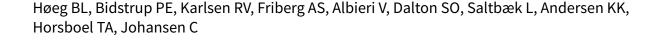


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# Follow-up strategies following completion of primary cancer treatment in adult cancer survivors (Review)



Høeg BL, Bidstrup PE, Karlsen RV, Friberg AS, Albieri V, Dalton SO, Saltbæk L, Andersen KK, Horsboel TA, Johansen C. Follow-up strategies following completion of primary cancer treatment in adult cancer survivors. *Cochrane Database of Systematic Reviews* 2019, Issue 11. Art. No.: CD012425. DOI: 10.1002/14651858.CD012425.pub2.

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# TABLE OF CONTENTS

ABSTRACT	1
PLAIN LANGUAGE SUMMARY	2
SUMMARY OF FINDINGS	4
BACKGROUND	12
Figure 1	13
OBJECTIVES	14
METHODS	14
Figure 2	16
RESULTS	19
Figure 3	22
Figure 4	26
Figure 5	29
Figure 6.	30
DISCUSSION	32
AUTHORS' CONCLUSIONS	35
ACKNOWLEDGEMENTS	36
REFERENCES	37
CHARACTERISTICS OF STUDIES	54
DATA AND ANALYSES	152
Analysis 1.1. Comparison 1 Non-specialist-led versus specialist-led follow-up, Outcome 1 Overall Survival	153
Analysis 1.2. Comparison 1 Non-specialist-led versus specialist-led follow-up, Outcome 2 EORTC-C30 - Global health status	154
Analysis 1.3. Comparison 1 Non-specialist-led versus specialist-led follow-up, Outcome 3 EORTC-C30 - Physical functioning	154
Analysis 1.4. Comparison 1 Non-specialist-led versus specialist-led follow-up, Outcome 4 EORTC-C30 - Role functioning	154
Analysis1.5.Comparison1Non-specialist-ledversusspecialist-ledfollow-up, Outcome5EORTC-C30-Emotionalfunctioning.	155
Analysis1.6.Comparison1Non-specialist-ledversusspecialist-ledfollow-up, Outcome6EORTC-C30-Cognitivefunctioning..	155
Analysis 1.7. Comparison 1 Non-specialist-led versus specialist-led follow-up, Outcome 7 EORTC-C30 - Social functioning	155
Analysis 1.8. Comparison 1 Non-specialist-led versus specialist-led follow-up, Outcome 8 STAI - State anxiety subscale	156
Analysis 1.9. Comparison 1 Non-specialist-led versus specialist-led follow-up, Outcome 9 HADS - Anxiety subscale	156
Analysis 1.10. Comparison 1 Non-specialist-led versus specialist-led follow-up, Outcome 10 HADS - Depression subscale	156
Analysis 2.1. Comparison 2 Less intensive versus more intensive follow-up, Outcome 1 Overall survival	157
Analysis 2.2. Comparison 2 Less intensive versus more intensive follow-up, Outcome 2 Time-to-detection of recurrence	157
ADDITIONAL TABLES	158
APPENDICES	162
CONTRIBUTIONS OF AUTHORS	174
DECLARATIONS OF INTEREST	174
SOURCES OF SUPPORT	174
DIFFERENCES BETWEEN PROTOCOL AND REVIEW	174
NOTES	175
INDEX TERMS	175



[Intervention Review]

# Follow-up strategies following completion of primary cancer treatment in adult cancer survivors

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#### **ABSTRACT**

# **Background**

Most cancer survivors receive follow-up care after completion of treatment with the primary aim of detecting recurrence. Traditional follow-up consisting of fixed visits to a cancer specialist for examinations and tests are expensive and may be burdensome for the patient. Follow-up strategies involving non-specialist care providers, different intensity of procedures, or addition of survivorship care packages have been developed and tested, however their effectiveness remains unclear.

# **Objectives**

The objective of this review is to compare the effect of different follow-up strategies in adult cancer survivors, following completion of primary cancer treatment, on the primary outcomes of overall survival and time to detection of recurrence. Secondary outcomes are health-related quality of life, anxiety (including fear of recurrence), depression and cost.

# Search methods

We searched CENTRAL, MEDLINE, Embase, four other databases and two trials registries on 11 December 2018 together with reference checking, citation searching and contact with study authors to identify additional studies.

#### **Selection criteria**

We included all randomised trials comparing different follow-up strategies for adult cancer survivors following completion of curatively-intended primary cancer treatment, which included at least one of the outcomes listed above. We compared the effectiveness of: 1) non-specialist-led follow-up (i.e. general practitioner (GP)-led, nurse-led, patient-initiated or shared care) versus specialist-led follow-up; 2) less intensive versus more intensive follow-up (based on clinical visits, examinations and diagnostic procedures) and 3) follow-up integrating additional care components relevant for detection of recurrence (e.g. patient symptom education or monitoring, or survivorship care plans) versus usual care.

# **Data collection and analysis**

We used the standard methodological guidelines by Cochrane and Cochrane Effective Practice and Organisation of Care (EPOC). We assessed the certainty of the evidence using the GRADE approach. For each comparison, we present synthesised findings for overall survival and time to detection of recurrence as hazard ratios (HR) and for health-related quality of life, anxiety and depression as mean differences



(MD), with 95% confidence intervals (CI). When meta-analysis was not possible, we reported the results from individual studies. For survival and recurrence, we used meta-regression analysis where possible to investigate whether the effects varied with regards to cancer site, publication year and study quality.

#### **Main results**

We included 53 trials involving 20,832 participants across 12 cancer sites and 15 countries, mainly in Europe, North America and Australia. All the studies were carried out in either a hospital or general practice setting. Seventeen studies compared non-specialist-led follow-up with specialist-led follow-up, 24 studies compared intensity of follow-up and 12 studies compared patient symptom education or monitoring, or survivorship care plans with usual care. Risk of bias was generally low or unclear in most of the studies, with a higher risk of bias in the smaller trials.

#### Non-specialist-led follow-up compared with specialist-led follow-up

It is uncertain how this strategy affects overall survival (HR 1.21, 95% CI 0.68 to 2.15; 2 studies; 603 participants), time to detection of recurrence (4 studies, 1691 participants) or cost (8 studies, 1756 participants) because the certainty of the evidence is very low.

Non-specialist- versus specialist-led follow up may make little or no difference to health-related quality of life at 12 months (MD 1.06, 95% CI-1.83 to 3.95; 4 studies; 605 participants; low-certainty evidence); and probably makes little or no difference to anxiety at 12 months (MD -0.03, 95% CI-0.73 to 0.67; 5 studies; 1266 participants; moderate-certainty evidence). We are more certain that it has little or no effect on depression at 12 months (MD 0.03, 95% CI-0.35 to 0.42; 5 studies; 1266 participants; high-certainty evidence).

#### Less intensive follow-up compared with more intensive follow-up

Less intensive versus more intensive follow-up may make little or no difference to overall survival (HR 1.05, 95% CI 0.96 to 1.14; 13 studies; 10,726 participants; low-certainty evidence) and probably increases time to detection of recurrence (HR 0.85, 95% CI 0.79 to 0.92; 12 studies; 11,276 participants; moderate-certainty evidence). Meta-regression analysis showed little or no difference in the intervention effects by cancer site, publication year or study quality.

It is uncertain whether this strategy has an effect on health-related quality of life (3 studies, 2742 participants), anxiety (1 study, 180 participants) or cost (6 studies, 1412 participants) because the certainty of evidence is very low. None of the studies reported on depression.

# Follow-up strategies integrating additional patient symptom education or monitoring, or survivorship care plans compared with usual care:

None of the studies reported on overall survival or time to detection of recurrence.

It is uncertain whether this strategy makes a difference to health-related quality of life (12 studies, 2846 participants), anxiety (1 study, 470 participants), depression (8 studies, 2351 participants) or cost (1 studies, 408 participants), as the certainty of evidence is very low.

# **Authors' conclusions**

Evidence regarding the effectiveness of the different follow-up strategies varies substantially. Less intensive follow-up may make little or no difference to overall survival but probably delays detection of recurrence. However, as we did not analyse the two outcomes together, we cannot make direct conclusions about the effect of interventions on survival after detection of recurrence. The effects of non-specialist-led follow-up on survival and detection of recurrence, and how intensity of follow-up affects health-related quality of life, anxiety and depression, are uncertain. There was little evidence for the effects of follow-up integrating additional patient symptom education/monitoring and survivorship care plans.

### PLAIN LANGUAGE SUMMARY

# Follow-up strategies after completion of primary cancer treatment

# What is the aim of this review?

In this Cochrane Review, we aimed to find out if cancer survivors who received three different types of follow-up care, after they were treated for their cancer, have better medical and personal outcomes. We collected and assessed all relevant studies and found 53 studies.

# **Key messages**

Non-specialist-led follow-up, such as follow-up provided by a general practitioner (GP) or nurse, makes little or no difference to health-related quality of life, anxiety or depression, when compared to specialist-led follow-up. We cannot be sure about its effects on overall survival and detection of a cancer returning after treatment (recurrence).

Less intensive follow-up, such as follow-up with fewer examinations or tests, may make little or no difference to overall survival but probably delays detection of recurrence when compared to more intensive follow-up. However, other types of studies are needed before



we can be certain about the effects of early detection of recurrence on survival. We also cannot be sure about its effect on health-related quality of life, anxiety and depression.

There was little evidence for the final type of follow-up, which integrated additional components relevant for detection of recurrence, such as patient symptom education or monitoring, or survivorship care plans.

#### What was studied in the review?

After being treated for cancer, most patients receive follow-up care to look for signs of recurrence. If the cancer returns, it is thought to be better to detect it earlier, as it allows earlier treatment, which is expected to improve survival for the patient. Traditional follow-up involving fixed visits to a cancer specialist in a hospital setting for examinations and tests can be expensive and burdensome for the patient. Newer follow-up strategies involving non-specialist care providers, different intensity of examinations, or the addition of survivorship care plans have been developed and tested but their effectiveness remains unclear.

The aim of our review was to find out if three types of aftercare increased survival, decreased the time until recurrence is detected, and improved patient outcomes such as health-related quality of life, anxiety and depression, as well as cost. The types of aftercare were: 1) non-specialist-led (e.g. GP-led, nurse-led, patient-initiated or shared care) versus specialist-led follow-up; 2) less intensive versus more intensive follow-up (based on frequency or intensity of clinical visits, examinations or diagnostic procedures); and 3) follow-up integrating additional care components relevant for detection of recurrence (e.g. patient symptom education or monitoring, or survivorship care plans) versus usual care.

#### What are the main results of the review?

We analysed 53 studies, involving 20,832 participants with 12 types of cancer in 15 different countries, mainly in Europe, North America and Australia. All the studies were carried out in either a hospital or general practice setting.

#### When cancer survivors receive aftercare led by non-specialists, such as GPs and nurses:

- We are not sure if overall survival is affected or if cancer recurrence is detected earlier:
- It probably makes little or no difference to health-related quality of life and anxiety and it makes no difference for depression at 12 months of follow-up;
- We are not sure there is a difference in costs between these two types of follow-up strategies.

#### When cancer survivors receive less intensive aftercare, such as fewer examinations and tests:

- It may make little or no difference to overall survival but it probably delays detection of recurrence;
- We are not sure if makes a difference to health-related quality of life, anxiety and costs. We did not find any studies assessing depression.

# When cancer survivors receive aftercare with additional education about their symptoms or survivorship care plans:

- We are not sure about how this type of aftercare improves health-related quality of life, anxiety or depression, or if increases the costs of care. We did not find any studies that assessed overall survival or if cancer recurrence is detected earlier.

# How up to date is this review?

We reviewed studies that had been published up to 11 December 2018.

# SUMMARY OF FINDINGS

Summary of findings for the main comparison. Non-specialist-led versus specialist-led follow-up after primary cancer treatment

# Non-specialist-led versus specialist-led follow-up after primary cancer treatment

**Patient or population:** adult cancer survivors from the following cancer sites: breast, colon, colorectal, endometrial, ovarian, cervical, melanoma and oesophageal **Setting**: outpatient treatment in hospitals or general practice in Australia, Canada, Denmark, Netherlands, Norway, Sweden and UK

**Intervention**: non-specialist-led (i.e. GP-led, nurse-led, patient-initiated or shared care) follow-up

**Comparison**: specialist-led follow-up

Outcomes	Anticipated abso (95% CI)	olute effects*	Relative ef- fects (95% CI)	Number of par- ticipants <sup>a</sup> (Number of	Certainty of the evidence (GRADE)	Comments		
	Risk with spe-Risk with non- cialist-led fol-specialist-led low-up follow-up			studies)	(GRADE)			
Overall survival Follow-up	89 per 100 <sup>b</sup> 87 per 100 (79 to 93)  Difference: 2 fewer survivors in the intervention group per 100 participants (between 10 fewer to 4 more)		HR 1.21 (0.68 to 2.15)	603 participants (2 randomised	⊕⊝⊝⊝ Very low <sup>c</sup>	4 studies reported on overall survival. It is uncertain how non-specialist-led follow-up affects overall survival as the certainty of the evidence is very low.		
range: 12 months to 60 months				trials)		We could not incorporate data from 2 other studies (N =1077) in the meta-analysis, both reported little or no difference in overall survival.		
Time to detection of recurrence Follow-up range: 3 months			See comment	1691 partici- pants (4 ran- domised trials)	⊕ooo Very low <sup>d</sup>	4 studies reported on time to detection of recurrence. It is uncertain how non-specialist-led follow-up affects time to detection of recurrence as the certainty of the evidence is very low and we could not pool the reported data.		
to 60 months						3 studies reported little or no difference in time to detection of recurrence and 1 study reported median time to recurrence but did not carry out any statistical analysis.		
Health-related quality of life, (at 12 months' follow-up)	-	-	MD 1.06 higher (1.83 lower to 3.95 higher)	605 participants (4 randomised trials)	⊕⊕⊙⊝ Low <sup>e</sup>	Thirteen studies reported on HRQoL using EORTC-C30, SF-36, SF-12, EuroQoL-5D and FACT at different time points. Meta-analysis of 4 studies showed that non-specialist-led follow-up may make little or no difference in		
EORTC-C30 global health status scale						HRQoL at 12 months as measured by the EORTC-C30 global health status scale. The mean difference did not reach the minimal clinically important difference of 10 points identified for this scale.		

(higher scores indicate better HRQoL)					Studies that we could not incorporate in the meta- analysis (N = 2385) generally reported that non-special- ist-led follow-up made little or no difference to HRQoL.
Anxiety (at 12 months' follow-up)  HADS-Anxiety subscale (higher scores indicate worse anxiety)		MD 0.03 lower (0.73 lower to 0.67 higher)	1266 participants (5 randomised trials)	⊕⊕⊕⊝ Moderate <sup>f</sup>	12 studies reported on anxiety and 2 on fear of recurrence using STAI, HADS and FCRI at different time points. Meta-analysis of 5 studies showed that non-specialist-led follow-up probably makes little or no difference to anxiety at 12 months as measured by HADS-Anxiety subscale. The mean difference did not reach the minimal clinically important difference of 1.5 points identified for this scale.  Data from the studies that we could not incorporate in the meta-analysis (N = 1755) generally reported that non-specialist-led follow-up made little or no difference to anxiety and fear of recurrence, except 1 study reporting higher levels of fear of recurrence in the patient-initiated follow-up group.
Depression (at 12 months) HADS-Depres- sion subscale (higher scores indicate worse depression)	-	MD 0.03 higher (0.35 lower to 0.42 higher)	1266 participants (5 randomised trials)	⊕⊕⊕⊕ Highg	Eleven studies reported on depression using GHQ-12 and HADS at different time points. Meta-analysis of 5 studies showed that non-specialist-led follow-up makes little or no difference to depression at 12 months as measured by HADS-Depression subscale. The mean difference did not reach the minimal clinically important difference of 1.5 points identified for this scale.  The studies that we could not incorporate in the meta-analysis (N = 1378) generally reported that non-specialist-led follow-up may make little or no difference to depression.
Cost	- See comment	-	1756 partici- pants (8 ran- domised trials)	⊕⊝⊝ Very low <sup>h</sup>	Eight studies reported cost outcomes but due to the substantial heterogeneity in how they measured and reported them, we could not pool the results in a meta-analysis. It is uncertain whether non-specialist-led follow-up has an effect on cost when compared with specialist-led follow-up, as the certainty of the evidence is very low.  6 studies reported lower cost per participant in the non-specialist-led group, while 2 studies reported higher cost per participant in the non-specialist-led group.

<sup>\*</sup>The basis for the assumed risk in the comparison group (assumed comparator risk, ACR) is provided in the footnotes. The corresponding risk in the intervention group (and its 95%confidence interval) is based on the ACR and the relative effect of the intervention (and its 95%CI).

#### **GRADE Working Group grades of evidence**

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

**Moderate certainty:** we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect

Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

<sup>a</sup>From meta-analysis if we pooled study results; for all studies if we did not pool study results.

<sup>b</sup>The ACR is the assumed proportion of participants who are alive in the comparison group.

<sup>c</sup>We judged the certainty of evidence to be very low and downgraded by three levels for very serious concerns regarding indirectness and imprecision, as representativeness is limited with only two studies, the HRs were not reported but indirectly estimated and the confidence interval was very wide.

dWe judged the certainty of evidence to be very low and downgraded by three levels for serious concerns regarding inconsistency, indirectness and imprecision due to few studies, reporting of results by different estimates that could not be pooled and high variance of the result estimates.

<sup>e</sup>We judged the certainty of evidence to be low and downgraded by two levels for serious concerns regarding inconsistency and imprecision due to differing estimates of effect and wide confidence intervals.

fWe judged the certainty of evidence to be moderate as we downgraded by one level for concerns regarding inconsistency of results and indirectness due to few studies. BWe judged the certainty of evidence to be high although we had some concerns regarding indirectness due to few studies.

hWe judged the certainty of evidence to be very low as the high heterogeneity led to serious concerns regarding inconsistency, indirectness and imprecision in the way cost outcomes were measured and reported across studies.

# Summary of findings 2. Less intensive versus more intensive follow-up after primary cancer treatment

# Less compared with more intensive components in follow-up after primary cancer treatment

Patient or population: adult cancer survivors from the following cancer sites: breast, colorectal, head-and-neck, Hodgkin lymphoma, melanoma, non-small cell lung cancer and testicular cancer

**Setting**: outpatient treatment in hospitals in Australia, Denmark, China, Finland, France, India, Italy, Netherlands, Spain, Sweden, Switzerland and UK **Intervention**: less intensive follow-up (based on fewer clinical visits, examinations or less intensive diagnostic procedures)

**Comparison**: more intensive follow-up

Outcomes	Anticipated absolute effects* (95% CI)	Relative ef- fects - (95% CI)	Number of par- ticipants <sup>a</sup> (Number of	Certainty of the evidence (GRADE)	Comments
	Risk with more Risk with less intensive follow-up low-up	(50% 0.1)	studies)	(5.2.2.4)	

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	Overall survival  Follow-up range: 24 months to 120 months	intervention grou	74 per 100 (72 to 76)  ver survivor in the up per 100 partici-3 fewer to 1 more)	(0.96 to 1.14) pants (13 ra trials) (0.96 to 1.14) pants		⊕⊕⊝⊝ Low <sup>c</sup>	18 studies reported on overall survival. Meta-analysis of 13 studies showed that less intensive follow-up may make little or no difference to overall survival. Meta-regression analysis showed little or no difference in the intervention effects by cancer site, publication year or study quality.  We could not incorporate data from 5 other studies. 3 of these studies reported little or no difference in overall survival (N = 1752), while 2 studies reported improved survival with more intensive follow-up (N = 544).
	Time to detection of recurrence Follow-up range: 12 months to 120 months	27 per 100d  Difference: 3 few recurrence in th group per 100 pt tween 5 to 2 few	e intervention articipants (be-	HR 0.85 (0.79 to 0.92)	11,276 participants (12 randomised trials)	⊕⊕⊕⊝ Moderate <sup>e</sup>	22 studies reported on time to detection of recurrence. Meta-analysis of 12 studies showed that less intensive follow-up probably increases time to detection of recurrence. Meta-regression analysis showed little or no difference in the intervention effects by cancer site, publication year or study quality.  We could not incorporate data from 10 other studies. 4 of these studies reported shorter time to detection of recurrence for more intensive follow-up (N = 854), while 4 other studies reported little or no difference in detection of recurrence (N = 734). 1 study reported results that we could not use for this comparison (N = 337) and 1 study reported results based on only unresectable recurrence (N = 239).
· · · · · · · · · · · · · · · · · · ·	Health-related quality of life	-	See comment	-	2742 partici- pants (3 ran- domised trials)	⊕ooo Very low <sup>f</sup>	3 studies reported on HRQoL using SF-36 and SF-12 at varying time points. We could not pool the reported data. It is uncertain whether less intensive follow-up has an effect on HRQoL when compared with more intensive follow-up, as the certainty of the evidence is very low.  All 3 studies reported that less intensive follow-up may make little or no difference in HRQoL when compared to more intensive follow-up at time points ranging from 12 months to 5 years.
	Anxiety	-	See comment	-	180 partici- pants (1 ran- domised trial)	⊕ooo Very low <sup>g</sup>	One study reported that less intensive follow-up may make little or no difference to anxiety at 12 months follow-up using STAI.  It is uncertain whether less intensive follow-up has an effect on anxiety when compared with more intensive follow-up, as the certainty of the evidence is very low.

Depression		-	-	-	None of the studies reported depression.					
Cost	- See comment	-	1412 partici- pants (6 ran- domised trials)	ФООО Very low <sup>h</sup>	6 studies reported cost outcomes but due to the substantial heterogeneity in how they measured and reported this outcome, we could not pool the results in a meta-analysis. It is uncertain whether less intensive follow-up has an effect on cost when compared with more intensive follow-up, as the certainty of the evidence is very low.  All studies report lower costs for the less intensive arm from the perspective of the participant or healthcare system but the difference in cost varied considerably depending on the components/procedures used in the different interventions.					

<sup>\*</sup>The basis for the assumed risk in the comparison group (assumed comparator risk, ACR) is provided in the footnotes. The corresponding risk in the intervention group (and its 95%confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95%CI).

CI: confidence interval; HR: hazard ratio; HRQoL: health-related quality of life; SF-36: Short Form Health Survey-36 items; SF-12: Short Form Health Survey-12 items; STAI: State Trait Anxiety Inventory

# **GRADE Working Group grades of evidence**

**High certainty:** we are very confident that the true effect lies close to that of the estimate of the effect.

**Moderate certainty:** we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect

Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

aFrom meta-analysis if we pooled study results; for all studies if we did not pool study results.

<sup>b</sup>The ACR is the assumed proportion of participants who are alive in the comparison group.

cWe judged the certainty of evidence to be low as we downgraded by two levels for some concerns regarding study limitations (lack of allocation concealment in one study) and indirectness as the studies were primarily investigating follow-up after colorectal and breast cancer, and serious concerns regarding imprecision as the confidence interval includes effects that are not trivial (potentially up to 3 fewer survivors per 100 participants).

dThe ACR is the assumed proportion of participants with a detected recurrence in the comparison group.

eWe judged the certainty of evidence to be moderate as we downgraded by one level for serious concerns regarding indirectness as seven of the studies did not report hazard ratios, so we indirectly estimated them from published data.

fWe judged the certainty of evidence to be very low and downgraded by three levels for serious concerns regarding inconsistency, indirectness and imprecision due to the few studies, heterogeneous measures and reporting of results by different estimates that we could not pool.

gWe judged the certainty of evidence to be very low and downgraded by three levels for serious concerns regarding inconsistency, indirectness and imprecision since there was only one study.

hWe judged the certainty of evidence to be very low and downgraded by three levels as the substantial heterogeneity led to serious concerns regarding inconsistency, indirectness and imprecision in the way cost was measured and reported across studies.



**Patient or population:** adult cancer survivors from the following cancer sites: breast, colorectal, endometrial, ovarian and prostate cancer **Setting**: outpatient treatment in hospitals or general practice in Australia, Canada, Netherlands, Sweden and USA

**Intervention:** follow-up integrating additional components relevant for detection of recurrence (e.g. patient symptom education or monitoring, or survivorship care plans (SCP))

Comparison: usual care

Outcomes	Anticipated abso (95% CI)	olute effects*	Relative ef- fects - (95% CI)	№ of studies	Certainty of the evidence (GRADE)	Comments		
	Risk with usual care	Risk with fol- low-up inte- grating addi- tional patient symptom ed- ucation/moni- toring or SCP	(50% 64)		(3.0.5-7)			
Overall sur- vival	-	-	-	-	-	None of the studies reported overall survival.		
Time-to- de- tection of re- currence	-	-	-	-	-	None of the studies reported detection of recurrence.		
Health-related quality of life, (HRQoL)	-	See comment	-	2846 participants (12 randomised trials)	⊕⊙⊙⊝ Very low <sup>a</sup>	12 studies reported on HRQoL using EORTC-C30, SF-36, SF-12, FACT and City of Hope QoL scale at varying time points. We could not pool the reported data. It is uncertain whether follow-up integrating additional patient symptom education/monitoring or SCP has an effect on HRQoL when compared with usual care, as the certainty of the evidence is very low.  11 studies reported that follow-up integrating additional patient education/SCP may make little or no difference to HRQoL when compared to usual care at fol-		
						low-up ranging from 6 months to 12 months. 1 study reported that SCP and patient coaching improved HRQoL at 3 months' follow-up.		
Anxiety	-	See comment		See comment		470 partici- pants (1 ran- domised trial)	⊕⊝⊝⊝ Very low <sup>b</sup>	One study reported that SCP may make little or no difference to anxiety at 12 months' follow-up using HADS.

				It is uncertain whether follow-up integrating additional patient symptom education/monitoring or SCP has an effect on anxiety when compared with usual care, as the certainty of the evidence is very low.
Depression	- See comment	- 2351 partici- pants (8 ran- domised trials)	⊕⊕⊝⊝ Very low <sup>c</sup>	8 studies reported on depression using HADS, POMS, PHQ-9, BSI-18, CES-D and the distress thermometer at varying time points. We could not pool the reported data. It is uncertain whether follow-up integrating additional patient symptom education/monitoring or SCP has an effect on depression when compared with usual care, as the certainty of the evidence is very low.  7 studies reported that follow-up integrating additional patient education/SCP may make little or no difference to depression when compared to usual care at follow-up ranging from 3 months to 12 months. 1 study reported that the intervention improved symptoms of depression at 12 months' follow-up.
Cost	- See comment	- 408 partici- pants (1 ran- domised trial)	⊕⊝⊝ Very low <sup>d</sup>	One study reported that the use of SCP make little or no difference to cost at 2 years' follow-up.  It is uncertain whether follow-up integrating additional patient symptom education/monitoring or SCP has an effect on cost when compared with usual care, as the certainty of the evidence is very low.

<sup>\*</sup>The corresponding risk in the intervention group (and its 95%confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95%CI).

**BSI-18:** Brief Symptom Inventory-18 items, **CES-D:** Center for Epidemiological Studies-Depression scale; **CI:** confidence interval; **EORTC-C30:** European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire; **FACT:** Functional Assessment of Cancer Therapy scale; **HADS:** Hospital Anxiety and Depression Scale; **HRQoL:** health-related quality of life; **PHQ-9:** Patient Health Questionaire-9 items; **POMS:** Profile of Mood States; **QoL:** quality of life; **SCP:** survivorship care plans; **SF-36:** Short Form Health Survey-36 items; **SF-12:** Short Form Health Survey-12 items

#### **GRADE Working Group grades of evidence**

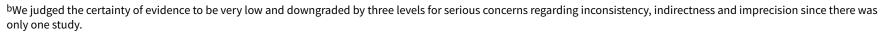
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

**Moderate certainty:** we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect

Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

<sup>q</sup>We judged the overall certainty of evidence to be very low and downgraded by three levels for serious concerns regarding study limitations, indirectness and imprecision due to studies being at high risk of bias, the heterogeneous measures and reporting of results by different estimates that could not be pooled.



<sup>c</sup>We judged the overall certainty of evidence to be very low and downgraded by three levels for serious concerns regarding study limitations, indirectness and imprecision due to one study at high risk of bias, the heterogeneous measures and reporting of results by different estimates that could not be pooled.

dWe judged the certainty of evidence to be very low and downgraded by three levels for serious concerns regarding inconsistency, indirectness and imprecision since there was only one study.



#### BACKGROUND

#### **Description of the condition**

Cancer has become a leading cause of death worldwide. Over 14 million new cases of cancer currently occur each year, and the World Health Organization expects this figure to rise by 70% over the next two decades (World Cancer Report 2014). Coupled with ever-improving screening programmes and cancer treatment procedures, these numbers are resulting in a burgeoning population of cancer survivors, who are channeled into many years of routine follow-up care after they have completed their primary cancer treatment (Davies 2011). In many countries, cancer is increasingly being managed as a chronic disease (Rose 2009).

Cancer is heterogeneous, with a range of cancer types, treatments, and outcomes. We will limit this review to the adult population, as childhood cancers differ biologically and aetiologically from adult cancers, resulting in different treatments and follow-up issues (Bleyer 1990). The post-treatment physical and psychosocial sequelae experienced by adult cancer survivors vary greatly (Howell 2012). However, regardless of cancer site, key areas of concern for survivors include the development of recurrent or new cancers, late and long-term effects of cancer and its treatment, and psychosocial and functional issues, such as depression, fear of recurrence, and difficulties navigating aftercare services (Jorgensen 2015; Landier 2009). Cancer follow-up care has been developed to address these concerns and unsurprisingly, is becoming a complex intervention with increased utilisation of new strategies that attempt to meet patient needs, and be clinically

effective and cost-effective at the same time (Davies 2011; Rose 2009).

# **Description of the intervention**

Cancer follow-up refers to the process of care delivered after the completion of primary cancer treatment, with the main objective being surveillance and prompt detection of recurrence or new cancers, in order to optimise further treatment outcomes (Collins 2004). Secondary objectives of follow-up programmes include identifying and managing side and late effects of cancer and its treatment, providing informational and psychological support, and relevant referrals to rehabilitation and other healthcare services (Rose 2009). There is currently no formal definition of what a follow-up strategy is, even as follow-up interventions are becoming increasingly complex and comprise many elements that have been developed over the past few decades in order to meet the objectives stated above (Howell 2012). Thus, we define follow-up strategies as the co-ordination and organisation of these elements, and in Box 1, we systematically distinguish between the various elements, based on the 'Five Ws and one H' framework, and give existing examples of each: why follow-up intervention, who leads the intervention, where does it take place, when are visits scheduled, what is delivered in each session, and how is care delivered (Spencer-Thomas 2016). While the framework is typically associated with the discipline of journalism, we have found it may be applied to understand systematically the complexity of cancer follow-up strategies.

Box 1. Elements that make up cancer follow-up strategies

Follow-up question	Examples
Why follow-up intervention?	<ul> <li>Early detection of recurrence</li> <li>Identification and management of physical and psychological symptoms</li> </ul>
Who leads?	<ul> <li>Specialist-led (e.g. oncologist or surgeon)</li> <li>Nurse-led</li> <li>General practitioner (GP)-led</li> <li>Shared care</li> </ul>
Where do visits take place?	<ul><li>Primary care</li><li>Secondary care</li></ul>
When are visits scheduled?	<ul> <li>Calendar-based: fixed frequency, timing, and length of follow-up</li> <li>Patient-initiated, based on symptoms</li> </ul>
What is delivered?	<ul> <li>Surveillance components: physical examination, biochemical tests, imaging procedures, etc.</li> <li>Aftercare components: patient information, symptom education, survivorship care plans, referrals to other services, etc.</li> </ul>
How is care delivered?	<ul><li>Face-to-face</li><li>Technology-mediated: telephone, email, etc.</li></ul>

Routine follow-up programmes traditionally consist of fixed, specialist-led, face-to-face outpatient visits in a hospital setting, which are scheduled frequently during the first few years (usually every two to four months), when the risk of recurrence is the

highest, followed by longer intervals between visits in subsequent years, for up to 10 years or more (De Felice 2015). Appointments almost always consist of surveillance components aimed at detection of recurrence, such as clinical examinations, blood tests



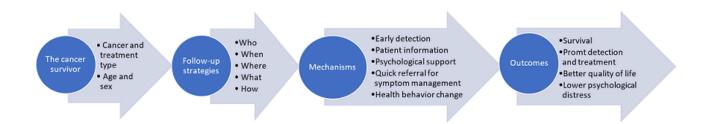
or imaging procedures, and also increasingly include aftercare components, such as patient education sessions, survivorship care plans and support in managing quality of life and psychosocial issues (Davies 2011). More intensive follow-up interventions have been defined by having more surveillance components in each appointment (Collins 2004). Certain aftercare components, such as symptom education and integration of a survivorship care plan in clinical care may also be expected to have an impact on detection of recurrence, as patients may be more likely to recognise and self-report signs of recurrence or adhere to follow-up visits.

Not surprisingly, cancer follow-up constitutes a heavy burden on national healthcare systems, and conventional specialist-led follow-up is increasingly unsustainable (Davies 2011). Therefore, other strategies, which are less comprehensive and may be more cost-effective, have been suggested, including: nurse-led follow-up, GP-led follow-up in primary care, patient-initiated follow-up, fewer appointments, and the use of less intensive tests and diagnostic procedures (Brown 2002; Dickinson 2014; Hall 2011; Oeffinger 2006; Rose 2009). Another area of research in cancer follow-up is the addition of survivorship packages that include patient education or information, such as a survivorship care plan (Jefford 2016). Regardless of follow-up strategy, the main aims continue to be surveillance aimed at early detection of recurrence, aftercare for late and long-term effects, and support for psychosocial and functional needs (Landier 2009). Expected outcomes for effective follow-up strategies are improved survival rates, prompt detection of recurrence, and better management of physical and psychological problems, leading to better quality of life for cancer survivors (Lewis 2009a). The current shift towards fewer visits with healthcare professionals and focus on patient empowerment, is also aimed at increasing survivors' capability to self-manage their condition and self-initiate contact with healthcare systems. However, this may increase anxiety and distress among survivors who lack the ability to self-monitor and self-manage (Lewis 2009a).

# How the intervention might work

Different mechanisms have been suggested to link the various components of follow-up interventions with their outcomes. Surveillance is based on the rationale that the earlier a cancer recurrence is detected, the more amenable it will be to treatment, and therefore, the higher the survival rate (Clarke 2014). However, few trials have studied these two outcomes together and currently, there is no strong evidence that routine surveillance improves time to detection of recurrence or overall survival (Clarke 2014; Jeffery 2016; Moschetti 2016). Furthermore, symptoms of recurrences are frequently detected by patients themselves, between scheduled visits, and traditional hospital-based appointments often fail to meet patients' supportive care needs (De Felice 2015). This has led to an increased focus on strategies where patients are trained to recognise, report, and self-manage symptoms of recurrence, late and long-term side-effects, emotional distress, and functional needs (Davies 2011). This may be achieved through patient information and symptom education programmes, psychosocial support provided by trained nurses, and quick referral to specialised care, rehabilitation, and other healthcare services when needed (Davies 2011). There is evidence that such strategies are positively accepted by patients, and may improve patientreported outcomes, such as health-related quality of life (Brennan 2011; Davies 2011). In Figure 1, we constructed a model that summarises the potential links between follow-up strategies, possible mechanisms, and expected outcomes. As illustrated, cancer-related factors (e.g. cancer type and treatment) and patientrelated factors (e.g. age and sex) determine the symptoms relevant to a particular patient group, which in turn, inform the organisation of the different elements within specific follow-up strategies. Therefore, follow-up strategies might work through different mechanisms for different patient groups, to achieve the expected outcomes of survival and symptom management.

Figure 1. Proposed model of cancer follow-up, mechanisms and possible outcomes



# Why it is important to do this review

Due to the rapidly rising numbers of cancer survivors, healthcare systems are under increasing pressure to optimise follow-up interventions to meet patients' physical, psychological, and functional needs, while remaining economically viable (Lewis

2009a). New models of follow-up care continue to be developed and implemented, affecting the lives of millions of survivors, but guidance for the development of effective follow-up strategies has been limited so far by the small number of randomised trials available for each cancer site and the heterogeneity



of these studies. The optimal content and organisation of follow-up procedures are still under debate (Sperduti 2013). Currently, four Cochrane Reviews on follow-up strategies have been published for specific cancer sites (breast cancer (Moschetti 2016), non-metastatic colorectal cancer (Jeffery 2016), cervical cancer (Lanceley 2013), and epithelial ovarian cancer (Clarke 2014)) but with the exception of the review on colorectal cancer follow-up, they have lacked the power to draw conclusions on the effects of different follow-up strategies due to the lack of studies. One Cochrane Review evaluated follow-up interventions regardless of type of cancer, but the focus was on interventions that improved continuity of care across the entire period of cancer treatment, and the outcomes of survival and recurrence were not included (Aubin 2012). This review sets out to fill this gap by including randomised trials of cancer follow-up strategies across all cancer sites. By doing so, we seek to overcome the limitation of low numbers of trials in certain sites and provide a systematic overview of the latest  $available\ evidence\ for\ follow-up\ strategies\ in\ multiple\ cancer\ types,$ including those that have not been previously represented (e.g. lung cancer, head and neck cancer, etc.).

#### **OBJECTIVES**

The objective of this review is to compare the effect of different follow-up strategies in adult cancer survivors, following completion of primary cancer treatment, on the primary outcomes of overall survival and time to detection of recurrence. Secondary outcomes are health-related quality of life, anxiety (including fear of recurrence), depression and cost.

#### METHODS

# Criteria for considering studies for this review

#### Types of studies

We included all randomised trials that compared different followup strategies in adult cancer survivors who had completed curatively intended primary cancer treatment, with respect to the outcomes of overall survival, time to detection of recurrence, health-related quality of life, depression, anxiety and cost. We did not put any restrictions on the language of the publication. Studies published in other languages were translated into English if necessary.

### **Types of participants**

We included trials that involved adults (18 years of age or older) who had completed curatively-intended primary cancer treatment. Participants must have been histologically and clinically diagnosed with cancer, regardless of cancer type and stage.

# **Types of interventions**

We included trials that compared any of the following interventions that might be expected to have an impact of detection of recurrence.

- Non-specialist-led follow-up (i.e. GP-led, nurse-led, patientinitiated or shared care) versus specialist-led follow-up
- Less intensive versus more intensive follow-up (based on clinical visits, examinations and diagnostic procedures)
- Follow-up integrating additional patient symptom education or monitoring, or survivorship care plans versus usual care

We excluded studies testing only psychosocial or rehabilitation components or studies investigating diagnostic components that were not integrated as part of clinical cancer follow-up.

#### Types of outcome measures

#### **Primary outcomes**

- Overall survival: calculated from time of randomisation or recruitment to study until time of death
- Time to detection of recurrence: calculated from time of randomisation or recruitment to study until detection of recurrence. In some studies, this outcome was called diseasefree survival.

#### Secondary outcomes

- · Health-related quality of life
- Anxiety (including fear of recurrence)
- Depression
- Cost

We included all studies that planned to report or reported on at least one of our outcome measures. We only considered health-related quality of life, anxiety and depression if studies measured them using validated scales, such as the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire for cancer patients (EORTC QLQ-C30; Aaronson 1993), the 36-item Short Form Health Survey (SF-36; Ware 1994), the Hospital Anxiety and Depression Scale (HADS; Snaith 2003), etc. For all included studies, we also extracted cost outcome data if they were reported.

#### Search methods for identification of studies

# **Electronic searches**

The review authors developed the search strategies in consultation with the Effective Practice and Organisation of Care (EPOC) Information Specialist (IS), who also ensured that the search strategy was peer-reviewed by a second IS. We searched the Cochrane Database of Systematic Reviews (CDSR) and the Database of Abstracts of Reviews of Effects (DARE) for related systematic reviews and the databases below for primary studies on 11 December 2018:

- Cochrane Central Register of Controlled Trials (CENTRAL; 2018, Issue 12) in the Cochrane Library
- MEDLINE Ovid, including Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Versions (1946 to 11 December 2018)
- Embase Ovid (1974 to 11 December 2018)
- PsycINFO Ovid (1967 to 11 December 2018)
- CINAHL EBSCO (Cumulative Index to Nursing and Allied Health Literature; 1982 to 11 December 2018)

Search strategies are comprised of keywords and controlled vocabulary terms. We applied no language or time limits. All strategies used are provided in Appendix 1.

### Searching other resources

We also searched the following registers for ongoing trials on 11 December 2018:



- International Clinical Trials Registry Platform (ICTRP), Word Health Organization (WHO), www.who.int/ictrp/en/
- ClinicalTrials.gov, US National Institutes of Health (NIH), ClinicalTrials.gov.

Additionally, we reviewed reference lists of all included studies and relevant systematic reviews, as well as contacted authors of relevant studies and reviews to clarify reported published information and to seek unpublished results and data.

### Data collection and analysis

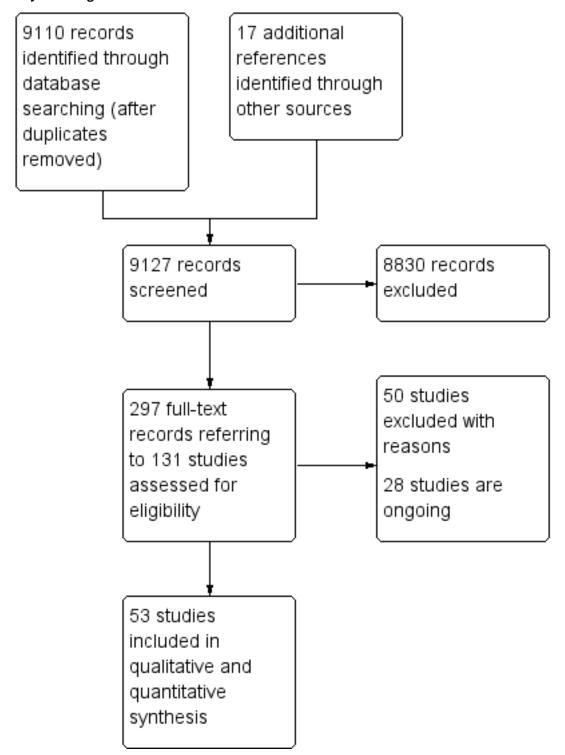
#### **Selection of studies**

We uploaded all titles and abstracts retrieved by electronic searching and through other sources into Covidence, which is an online platform that facilitates the management of the systematic

review process (Covidence). We used Covidence to carry out both the title/abstract screening stage and the full-text screening stage. Five review authors (BLH, RVK, LS, ASF and TAH) independently screened all titles and abstracts for inclusion and we obtained the full text of study reports and publications coded as "Yes" or "Maybe". Thereafter, the authors independently screened the full texts to identify studies for inclusion. We tagged excluded studies with the reason for exclusion, following a similar hierarchy as the screening algorithm: wrong intervention, wrong patient population (e.g. patients were not cancer-free or were treated for recurrence) or wrong outcome. These reasons are predefined in Covidence. We resolved any disagreements during both screening stages through regularly held discussion meetings with the rest of the author team. We also identified ongoing studies and recorded any information available. We extracted Information from Covidence regarding the selection process to complete a PRISMA flow diagram (Liberati 2009; Figure 2).



Figure 2. Study flow diagram



# **Data extraction and management**

We used a modified Cochrane data collection form from our editorial group, Cochrane Effective Practice and Organisation of Care (EPOC), to capture study characteristics and outcome data (EPOC 2013). We used the first five studies to pilot and refine the template. Five review authors (BLH, RVK, LS, ASF and TAH) extracted the following study characteristics from included studies.

- Methods: study design, number of study centres and location, study setting, withdrawals, date of study, follow-up
- Participants: cancer site, number, mean age, age range, gender, cancer stage, diagnostic criteria, inclusion criteria, exclusion criteria, other relevant characteristics
- Interventions: intervention type, intervention components, comparison, fidelity assessment



- Outcomes: main and other outcomes specified and collected, time points reported
- Notes: funding for trial, notable conflicts of interest of trial authors, and ethical approval

For each study, one review author extracted all the pre-defined relevant data and another review author independently read all the publications from the same study and double-checked the form to ensure accuracy and that there were no missing data. We only extracted outcome data for outcomes relevant for this review. For studies with multiple reports, we extracted data from all the reports, if relevant. We resolved any disagreements during discussion meetings with the rest of the review author team. To minimise error, the review authors used the guidance provided in Chapter 7 of the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011a), and took the online Cochrane Interactive Learning course on selecting studies and collecting data (Sambunjak 2017). We used information from the data collection forms to create the 'Characteristics of included studies' table. We noted if the study did not contribute data that could be pooled in a meta-analysis.

#### Assessment of risk of bias in included studies

Five review authors (BLH, RVK, LS, ASF and TAH) independently assessed risk of bias for each study, using the criteria outlined in Chapter 8 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2017) and guidance from EPOC (EPOC 2015). To further minimise error, the authors also took the Cochrane Interactive Learning course on introduction to study quality and risk of bias (Page 2017). We resolved disagreements by discussion with the rest of the author team or with the editors of this review. We assessed the risk of bias according to the following domains.

- Random sequence generation
- · Allocation concealment
- · Blinding of participants and personnel
- · Blinding of outcome assessment
- · Incomplete outcome data
- Selective outcome reporting
- Other bias, including baseline imbalances and risk of contamination

As the risk of detection bias differs for objective outcomes (survival and recurrence) and patient-reported outcomes (quality of life, anxiety and depression), we assessed the risk of bias by type of outcome for the following domains: blinding of participants and personnel, blinding of outcome assessment and incomplete outcome data (Higgins 2017). For blinding of outcome assessment, we further assessed the risk of bias separately for survival and time to detection of recurrence because while there can be no doubt as to death, time to detection of recurrence may be influenced by judgement regarding clinical tests and assessments, which may be affected by lack of blinding.

We classified each potential source of bias as high, low, or unclear, and provide a quote from the study report and justification for our judgement in the 'Risk of bias' table. When considering treatment effects, we took into account the risk of bias for the studies that contributed to that outcome.

#### Measures of treatment effect

#### Time-to-event outcomes

We have presented time-to-event outcomes, overall survival and time to detection of recurrence, as hazard ratios (HRs) (Deeks 2017). We estimated log HRs and the associated standard error (SE) required for a meta-analysis using the calculator in Review Manager 5 (Review Manager 2014) and a spreadsheet developed by Tierney 2007 that provides 11 methods for calculating HRs and the associated variance depending on the information available in each study. We used Method 3 for studies that provided a HR and its associated confidence interval (CI), Method 9 for studies that provided a P-value from a log-rank test, the number of events and the numbers randomised to each arm and Method 11 when a study only provided Kaplan-Meier curves and numbers at risk. For multi-armed studies, we also used the approach proposed by Parmar 1998 to estimate the overall log HR and its variance for the combined intervention arms. We also contacted the authors of relevant studies for additional information where possible and noted this, along with any response, in the Characteristics of included studies.

We did not specify the minimal clinically important difference (MCID) (Patrick 2011) for survival and time to detection of recurrence for this review. Instead, we assessed the importance of effects and the precision of the estimates based on how likely it seemed to us that some people would make different decisions if the true effect was near one end or the other of the CI, for example, when the CI includes effects that are not trivial (EPOC 2018).

#### **Continuous outcomes**

For health-related quality of life, anxiety and depression, we calculated the mean difference (MD) for each measurement tool together with the 95% CI by using the mean final value scores and the associated standard deviations (SD) in each study (Deeks 2017). We used final value scores at 12 months as this was the time point reported by the majority of the included studies and because we considered one year a sufficient period of time to assess a meaningful effect of the intervention on patient-reported outcomes. We also used mean final value scores and the associated SDs instead of other estimates of treatment effects because this was the measurement most consistently reported across the included studies. We did not use the standardised mean difference (SMD) because the different scales/subscales often measure different dimensions of an outcome and combining the results would not be meaningful.

In the few studies where means and SDs were not reported, we attempted to contact the study author of for the required information. Where possible, we estimated the mean and SD using the methods described in Chapter 7 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011a), and in Wan 2014. For each measurement tool, we state the range of scores possible, whether an increase in score is desirable and the MCID, if available from the literature. Information regarding whether a study author was contacted, what information was requested, and whether we received a reply was noted in the Characteristics of included studies table.



#### Unit of analysis issues

We included cluster-randomised trials in the meta-analysis only if we were able to extract an estimate of the treatment effect from an analysis that properly accounted for the cluster design. For trials with multiple intervention groups, we only included the group with the intervention that met the inclusion criteria for this review (Kimman 2011), or we combined the intervention groups (Primrose 2014), and created a single pair-wise comparison with the control group for the meta-analysis. We did not include cross-over trials in this review.

# Dealing with missing data

We report missing data and attrition rates for the included studies as part of the 'Risk of bias' assessment under the domain 'Incomplete outcome data'. Where possible, we contacted study authors in order to verify key study characteristics and obtain unreported outcome data. Almost all the included studies reported intention-to-treat (ITT) analyses or methods to impute missing data, thus indicating an ITT approach. If a study reported both ITT and per-protocol analyses, we extracted only ITT outcome data. We did not impute missing data and we did not request individual patient data.

#### **Assessment of heterogeneity**

We used the Chi² test and the I² statistic (Higgins 2003), to measure statistical heterogeneity among the trials in the analysis for each outcome (Deeks 2017; Thompson 2002). We expected clinical heterogeneity, as there was substantial variation across studies on study and patient characteristics. Therefore, regardless of the statistical heterogeneity level, we planned and performed a random-effects meta-regression analysis, as reported below, to investigate prespecified study differences.

# **Assessment of reporting biases**

For outcomes where we were able to pool more than 10 studies, we created and examined a funnel plot to explore possible publication biases and interpreted the results with caution (Sterne 2011). For studies where a protocol had been published or the study had been prospectively registered, we compared the predefined outcome measures with those that the study reported as part of the risk of bias assessment under the domain 'Selective reporting'.

### **Data synthesis**

For time-to-event outcomes, we carried out a meta-analysis for all the trials where it was possible to estimate a log HR and associated sampling variance. We present relative effects (HR) and estimated anticipated absolute effects in terms of the absolute risk of event-free survival (i.e. the event being death) for overall survival, and as the absolute risk of an event for recurrence, based on formulae found in Schünemann 2019.

For continuous outcomes, we carried out a meta-analysis for each scale or subscale if at least three studies reported a measurement scale or subscale at 12 months' follow-up, in order to have reasonable representativeness and probability of detecting the effect of interest.

We synthesised data based on three intervention comparisons:

- 1. Non-specialist-led follow-up (i.e. GP-led, nurse-led, patient-initiated or shared care) versus specialist-led follow-up
- Less intensive versus more intensive follow-up (based on clinical visits, examinations and procedures). In trials where the intervention group received the more intensive treatment, the reported estimates for intervention and comparison arms were reversed.
- 3. Follow-up integrating additional patient symptom education or monitoring, or survivorship care plans versus usual care

In each comparison group, we followed the same procedures with regards to undertaking a possible meta-analysis and meta-regression analysis (see Subgroup analysis and investigation of heterogeneity). We carried out all meta-analyses in Review Manager 5 using the inverse variance random-effects method (Review Manager 2014). We carried out meta-regression in the statistical software R (version 3.5.1, package 'meta'; R 2017), and the codes are available in Appendix 2 . For the studies that reported data that we could not pool in the meta-analyses, we have presented the findings in a narrative manner (Deeks 2017).

#### 'Summary of findings' tables

For each intervention comparison, we used the GRADEpro software (GRADEpro GDT 2015), to create a 'Summary of findings' table for overall survival, time to detection of recurrence, health-related quality of life, anxiety, depression and cost. We assessed the overall certainty of evidence for each outcome using the five GRADE considerations: study limitations (risk of bias), consistency (of effect and measurement across studies), imprecision (wide confidence intervals in study estimates), indirectness (representativeness and whether we had to indirectly calculate effect estimates), and publication bias (through funnel plots if we pooled 10 or more studies; Schünemann 2013). We also used the methods and recommendations described in Section 8.5 (Higgins 2017), and Chapter 12 (Schünemann 2017), of the Cochrane Handbook for Systematic Reviews of Interventions and the EPOC worksheets (EPOC 2017), and attach the GRADE evidence profiles for each outcome in Appendix 3.

As we only included randomised trials, the evidence certainty started at 'high', If we identified any serious concerns in any of the five GRADE domains, we downgraded the certainty of the evidence accordingly by either one level to 'moderate.' two levels to 'low' or three levels to 'very low' (Guyatt 2008). Three review authors (BLH, RVK and ASF) carried out the GRADE assessments of each outcome and we resolved any disagreements with the rest of the review author group. For the outcomes of health-related quality of life, anxiety and depression, we presented the findings from the EORTC-C30 Global health status subscale, the HADS-Anxiety subscale and the HADS-Depression subscale, as we judged the results from these subscales to be most representative of the outcome. Additional outcome information that we were not able to incorporate into the evidence from the meta-analyses are noted in the comments section.

# Subgroup analysis and investigation of heterogeneity

An important aim of this review is to investigate how characteristics of all the different strategies may relate to outcome effects. Therefore, we investigated this heterogeneity by performing metaregression analysis, that is, including various predefined study characteristics as explanatory variables and testing for significance.



By doing so, we aimed to compare the effect of various follow-up strategies without splitting participant data into subgroups, where conclusions may be misleading if there are a limited number of studies available. To avoid false positive conclusions that can occur through post-hoc analyses, we identified the co-variates we wished to investigate a priori (Thompson 2002), and carried out a meta-regression analysis to investigate how the following variables relate to the primary outcomes of overall survival and time to detection of recurrence:

- · cancer site;
- · sex of participant;
- · age of participant;
- study quality (i.e. high (4-5 low 'Risk of bias' judgements); moderate (2-3 low 'Risk of bias' judgements); low (0-1 low 'Risk of bias' judgements));
- year of publication (i.e. before 2000; after 2000).

We note that associations derived from meta-regressions are observational, and that the risk of bias must be taken into account in the interpretation of results. Due to insufficient studies, we were not able to carry out meta-regression analyses for the continuous outcomes and we present our findings in a narrative manner (Deeks 2017). We did not carry out subgroup analysis.

### **Sensitivity analysis**

For each meta-analysis, we carried out a sensitivity analysis whereby we restricted the analysis to studies with published HRs, means and SD, and we noted their impact on effect sizes. We did not restrict the analysis to studies with low risk of bias, as we had already investigated the effect of study quality through meta-regression.

#### Assesment of bias in conducting the systematic review

We conducted this review according to the published protocol and report all deviations in the 'Differences between protocol and review' section below. We used PRISMA statement (Liberati 2009), to guide the reporting of this review.

#### RESULTS

# **Description of studies**

# Results of the search

After the removal of duplicates, the electronic search yielded 9110 references and we identified a further 17 references from other sources. Following title and abstract screening, we identified and retrieved the full text of 297 references and collated the references into 131 studies. Following full-text screening, we identified 81 studies for inclusion, of which 28 studies were ongoing (see Characteristics of included studies and Characteristics of ongoing studies tables). We excluded 50 studies with reasons (see Characteristics of excluded studies). The screening flow diagram and the proportions of included studies that contributed to each comparison and outcome can be seen in Figure 2 (Moher 2009).

# **Included studies**

Below, we provide a brief summary of the 53 included studies. Two of the included studies were cluster-randomised trials (Murchie 2010; ROGY 2015), and three studies were multi-armed (Kimman 2011; Primrose 2014; Secco 2002).

#### Participants, cancer site and setting

The included studies randomised 20,832 participants and spanned 12 cancer sites: 18 studies with participants who had breast cancer (Beaver 2009; Brown 2002; GIVIO 1994; Grunfeld 1996; Grunfeld 2006; Grunfeld 2011; Hershman 2013; Juarez 2013; Kimman 2011; Kirshbaum 2017; Koinberg 2004; Kokko 2003; Kvale 2016; Maly 2017; Oltra 2007; Rosselli Del Turco 1994; Ruddy 2016; Sheppard 2009), 16 studies in colorectal cancer (Beaver 2012; GILDA 2016; Jefford 2016; Kjeldsen 1997; Mäkelä 1992; Ohlsson 1995; Pietra 1998; Primrose 2014; Rodríguez-Moranta 2006; Schoemaker 1998; Secco 2002; Sobhani 2008; Sobhani 2018; Wang 2009; Wille-Jorgensen 2018; Young 2013), three studies in non-small cell lung cancer (NSCLC) (Gambazzi 2018; Monteil 2010; Westeel 2012), two studies in colon cancer (Augestad 2013; Wattchow 2006), two studies in endometrial cancer (Beaver 2017; Jeppesen 2018), two studies in gynaecological cancer (ROGY 2015; Morrison 2018), two studies in melanoma (Damude 2016; Murchie 2010), two studies with prostate cancer (Davis 2013; Emery 2016), two studies with oesophageal cancer (Malmstrom 2016; Verschuur 2009), and one study each in Hodgkin lymphoma (Picardi 2014), testicular cancer (Rustin 2007), head-and-neck cancer (Van der Meulen 2013) and oral cancer (D'Cruz 2016). The majority of the studies included participants with cancer stages I, II and III, while six studies also included participants with stage IV cancer at diagnosis, who had completed curatively-intended treatment (Gambazzi 2018; Picardi 2014; ROGY 2015; Sobhani 2008; Sobhani 2018; Verschuur 2009). The studies had follow-up periods ranging from six months to five years.

All the studies were carried out in either a hospital or general practice setting and 15 countries were represented: the UK (Beaver 2009; Beaver 2012; Beaver 2017; Brown 2002; Grunfeld 1996; Kirshbaum 2017; Morrison 2018; Murchie 2010; Primrose 2014; Rustin 2007; Sheppard 2009), Italy (GILDA 2016; GIVIO 1994; Picardi 2014; Pietra 1998; Rosselli Del Turco 1994; Secco 2002), Australia (Emery 2016; Jefford 2016; Schoemaker 1998; Wattchow 2006; Young 2013), the USA (Davis 2013; Hershman 2013; Juarez 2013; Kvale 2016; Maly 2017; Ruddy 2016), the Netherlands (Damude 2016; Kimman 2011; ROGY 2015; Van der Meulen 2013; Verschuur 2009), France (Monteil 2010; Sobhani 2008; Sobhani 2018; Westeel 2012), Canada (Grunfeld 2006; Grunfeld 2011), Denmark (Jeppesen 2018; Kjeldsen 1997; Wille-Jorgensen 2018), Sweden (Koinberg 2004; Malmstrom 2016; Ohlsson 1995), Finland (Kokko 2003; Mäkelä 1992), Spain (Oltra 2007; Rodríguez-Moranta 2006), China (Wang 2009), India (D'Cruz 2016), Norway (Augestad 2013), and Switzerland (Gambazzi 2018).

Nine studies did not report funding source (Brown 2002; Damude 2016; Koinberg 2004; Mäkelä 1992; Oltra 2007; Pietra 1998; Rustin 2007; Secco 2002; Wang 2009). The remaining studies were funded by either academic, public or non-profit sources, although two studies also reported contributions from industry (GIVIO 1994; Westeel 2012). Authors from six studies reported disclosures on potential conflicts of interests (Jefford 2016; Maly 2017; Primrose 2014; ROGY 2015; Ruddy 2016; Wille-Jorgensen 2018).

#### Types of interventions

The included studies investigated a wide range of interventions, and details of the types of interventions, comparisons and follow-up periods are given in the Characteristics of included studies tables.



Six studies compared nurse-led follow-up with conventional specialist-led follow-up (Beaver 2009; Beaver 2012; Beaver 2017; Kimman 2011; Morrison 2018; Verschuur 2009).

Five studies compared GP-led follow-up with conventional specialist-led follow-up (Augestad 2013; Grunfeld 1996; Grunfeld 2006; Murchie 2010; Wattchow 2006).

Five studies compared patient-initiated follow-up with conventional specialist-led follow-up (Brown 2002; Jeppesen 2018; Kirshbaum 2017; Koinberg 2004; Sheppard 2009). This type of follow-up was also referred to as 'open-access' or 'on-demand' follow-up in some of the publications.

One study compared shared care (where a number of hospital visits are replaced by GP-appointments) with conventional specialist-led follow-up (Emery 2016).

Four studies compared frequency of follow-up visits: one study compared fewer visits with more frequent visits (Damude 2016), while three compared more frequent visits with fewer visits (Kjeldsen 1997; Pietra 1998; Wille-Jorgensen 2018). When the latter three studies contributed data to the meta-analysis comparing less intensive to more intensive follow-up, we reversed the reported estimates for intervention and comparison arms.

Two studies compared a less intensive follow-up intervention to more intensive follow-up: Picardi 2014 compared follow-up based on the use of chest X-rays with follow-up using PET/CT scans in Hodgkin lymphoma survivors, while Rustin 2007 compared follow-up based on two CT scans with follow-up based on five CT scans in testicular cancer survivors.

Eighteen studies compared a more intensive follow-up intervention to less intensive follow-up based on the use of additional or more intensive surveillance components, for example, additional examinations, imaging procedures or blood tests for biomarkers (D'Cruz 2016; Gambazzi 2018; GILDA 2016; GIVIO 1994; Kokko 2003; Mäkelä 1992; Monteil 2010; Ohlsson 1995; Oltra 2007; Primrose 2014; Rodríguez-Moranta 2006; Rosselli Del Turco 1994; Schoemaker 1998; Secco 2002; Sobhani 2008; Sobhani 2018; Wang 2009; Westeel 2012). When these studies contributed data to the meta-analysis, we reversed the reported estimates for intervention and comparison arms.

Twelve studies investigated the addition of care or information components to usual care that might be expected to affect surveillance of recurrences, such as symptom monitoring and feedback (Davis 2013), implementation of survivorship care plans/packages in clinical care (Grunfeld 2011; Hershman 2013; Jefford 2016; Kvale 2016; Maly 2017; ROGY 2015; Ruddy 2016), or implementation of supportive care packages that included patient education on symptoms of recurrence (Juarez 2013; Malmstrom 2016; Van der Meulen 2013; Young 2013).

# Outcomes

#### Overall survival

Twenty-two studies reported on the outcome of overall survival (D'Cruz 2016; GILDA 2016; GIVIO 1994; Grunfeld 2006; Kjeldsen 1997; Koinberg 2004; Kokko 2003; Mäkelä 1992; Monteil 2010; Ohlsson 1995; Pietra 1998; Primrose 2014; Rodríguez-Moranta 2006; Rosselli Del Turco 1994; Schoemaker 1998; Secco 2002; Sobhani

2018; Verschuur 2009; Wang 2009; Wattchow 2006; Westeel 2012; Wille-Jorgensen 2018). Eight studies reported HRs (D'Cruz 2016; GILDA 2016; Rodríguez-Moranta 2006; Rosselli Del Turco 1994; Schoemaker 1998; Wang 2009; Westeel 2012; Wille-Jorgensen 2018), and we were able to calculate HRs for seven studies based on the information reported or obtained from the study authors (GIVIO 1994; Kjeldsen 1997; Koinberg 2004; Mäkelä 1992; Ohlsson 1995; Sobhani 2018; Wattchow 2006), thus yielding 15 studies that contributed data for meta-analysis. The remaining seven studies either did not carry out survival analysis or reported insufficient information to estimate a HR.

#### Time to detection of recurrence

Thirty studies reported on the outcome of time to detection of recurrence/disease-free survival (Augestad 2013; Beaver 2009; Beaver 2012; Beaver 2017; Damude 2016; Gambazzi 2018; GILDA 2016; GIVIO 1994; Grunfeld 1996; Grunfeld 2006; Kjeldsen 1997; Koinberg 2004; Kokko 2003; Mäkelä 1992; Monteil 2010; Ohlsson 1995; Oltra 2007; Picardi 2014; Pietra 1998; Primrose 2014; Rodríguez-Moranta 2006; Rosselli Del Turco 1994; Rustin 2007; Secco 2002; Sobhani 2008; Sobhani 2018; Wang 2009; Wattchow 2006; Westeel 2012; Wille-Jorgensen 2018). Four studies calculated time to detection of recurrence from the time of presentation of symptoms/suspicion of recurrence instead of from randomisation, as defined in our protocol, and we did not include the results from these studies in our analysis (Augestad 2013; Beaver 2009; Beaver 2012; Grunfeld 1996). Three study reported HRs (GILDA 2016; Westeel 2012; Wille-Jorgensen 2018), and we were able to calculate HRs for nine studies based on the information reported or obtained from the authors (Gambazzi 2018; GIVIO 1994; Kjeldsen 1997; Picardi 2014; Primrose 2014; Rodríguez-Moranta 2006; Rosselli Del Turco 1994; Rustin 2007; Sobhani 2008), thus yielding twelve studies that contributed data for the meta-analysis. The remaining studies either did not carry out survival analysis or reported insufficient information to estimate a HR.

# Health-related quality of life

Twenty-eight studies reported on the outcome of health-related quality of life using a variety of validated measurement scales, such as the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30; Augestad 2013; Beaver 2017; Brown 2002; Jefford 2016; Kimman 2011; Kirshbaum 2017; Malmstrom 2016; Morrison 2018; ROGY 2015; Verschuur 2009), the 36-item Short Form Health Survey (SF-36; Damude 2016; Grunfeld 1996; Grunfeld 2006; Grunfeld 2011; Kvale 2016; Murchie 2010), the 12-item Short Form Health Survey (SF-12; Davis 2013; GILDA 2016; Maly 2017; Ruddy 2016; Wattchow 2006), the Functional Assessment of Cancer Therapy - General (FACT-G; Davis 2013), Breast (FACT-B; Hershman 2013; Sheppard 2009), Colorectal (FACT-C); Young 2013), the EuroQol-5D (Augestad 2013; Verschuur 2009), and the City of Hope Quality of Life Questionnaire (Juarez 2013). An older study (GIVIO 1994), measured quality of life using a compilation of items selected from several quality-oflife instruments available in 1985. The results of the EORTC-C30, SF-36 and SF-12 are not reported as overall scores but by subscales measuring specific domains of health-related quality of life. We carried out a meta-analysis for results at 12 months for scales or subscales that were reported by at least three studies as specified in our Methods section under Data synthesis. We have reported the studies that contributed data to meta-analysis for each specific scale or subscale in the results section below.



#### **Anxiety**

Fourteen studies reported on the outcome of anxiety: five studies used the State Trait Anxiety Inventory (STAI; Beaver 2009; Beaver 2012; Beaver 2017; Damude 2016; Kimman 2011), and nine studies used the Hospital Anxiety and Depression Scale - Anxiety subscale (HADS-Anxiety; Brown 2002; Emery 2016; Grunfeld 1996; Grunfeld 2006; Kirshbaum 2017; Koinberg 2004; Murchie 2010; ROGY 2015; Wattchow 2006). Two studies reported on fear of recurrence: one using a three-item questionnaire that was still being tested (Sheppard 2009), and one using the Fear of Cancer Recurrence Inventory (Jeppesen 2018). We carried out a meta-analysis for results at 12 months for scales or subscales that were reported by at least three studies as specified in our Methods section under Data synthesis. We have reported the studies that contributed data to meta-analysis for each specific scale or subscale in the results section below.

#### Depression

Nineteen studies reported on the outcome of depression or psychological distress: nine studies used the Hospital Anxiety and Depression Scale - Depression subscale (HADS-Depression; Brown 2002; Emery 2016; Grunfeld 1996; Grunfeld 2006; Kirshbaum 2017; Koinberg 2004; Murchie 2010; ROGY 2015; Wattchow 2006), three used the General Heath Questionnaire (GHQ-12; Beaver 2009; Beaver 2012; Sheppard 2009), two studies each used the Center for Epidemiological Studies-Depression scale (CES-D; Hershman 2013; Van der Meulen 2013), and the Distress thermometer (Juarez 2013, Young 2013), one study each used the Patient Health Questionnaire (PHQ-9; Kvale 2016), the Profile of Mood States (POMS; Grunfeld 2011), and the Brief Symptom Inventory (BSI-18; Jefford 2016). We carried out a meta-analysis for results at 12 months only for scales or subscales that were reported by at least three studies as specified in our Methods section under Data synthesis. We have reported the studies that contributed data to meta-analysis for each specific scale or subscale in the results section below.

## Cost

Sixteen studies reported cost outcomes (Augestad 2013; Beaver 2009; Beaver 2017; Damude 2016; Grunfeld 1996; Grunfeld 2011;

Kimman 2011; Koinberg 2004; Kokko 2003; Monteil 2010; Morrison 2018; Oltra 2007; Picardi 2014; Rodríguez-Moranta 2006; Secco 2002; Verschuur 2009). However, there was high heterogeneity in how the studies measured and reported this outcome and we could not pool the results in a meta-analysis.

#### **Excluded studies**

We excluded 44 studies with reasons. Following recommendations from the Cochrane Handbook for Systematic Reviews of Interventions, we classified studies as excluded with reason only if they were studies one might reasonably expect to be eligible for inclusion (see Characteristics of excluded studies table; Higgins 2011a). We excluded studies if the intervention was not follow-up treatment after primary cancer treatment (wrong intervention; Chang 2013; Helgesen 2000; Majhail 2019; Mathew 2014; NCT03125070; NCT03360994; Ploos van Amstel 2016; Rustin 2010; Song 2018; Stanciu 2015; Visser 2015; Watson 2014), if the participants included patients who were not cancer-free or were being treated for a recurrence (wrong patient population; Holtedahl 2005; Lanceley 2017; Moore 2002; NCT01973946; NCT02200133; NCT02361099; NCT03056469; NCT03424837; NCT03608410; Puri 2018; Skolarus 2017; Van Rhijn 2011), if our primary or secondary outcomes of interest were not an outcome included by the study (wrong outcomes; Faithfull 2001; Gulliford 1997; Haq 2015; Jefford 2011; Lyu 2016; NCT00049465; NCT01824745; NCT02209415; NCT03271099; NCT03618017; Parker 2018; Smith 2016; Strand 2011; Wheelock 2015), or if it was not a standard randomised trial (wrong design; Rogers 2018; Samawi 2017; Verberne 2015). Two potential studies registered on the ClinicalTrials.gov trials registry were reported as being withdrawn (NCT01993901; NCT02655068), and one study was never started due to lack of funding (Kessler 2013).

# Risk of bias in included studies

Figure 3 shows the summary of the 'Risk of bias' assessments for all the included studies. Reasons for the authors' judgements are given for each study in the 'Risk of bias' tables under the Characteristics of included studies.



Figure 3. 'Risk of bias' summary: review authors' judgements about each 'Risk of bias' item for each included study. Blank items indicate that this type of outcome was not reported by the study

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias): Objective outcomes	Blinding of participants and personnel (performance bias): Patient-reported outcomes	Blinding of outcome assessment (detection bias): Overall survival	Blinding of outcome assessment (detection bias): Time-to-detection of recurrence	Blinding of outcome assessment (detection bias): Patient-reported outcomes	Incomplete outcome data (attrition bias): Objective outcomes	Incomplete outcome data (attrition bias): Patient-reported outcomes	Selective reporting (reporting bias)	Other bias
Augestad 2013	•	•	?	?		?	?	•	•	•	?
Beaver 2009	•	•	?	?		?	?	•	•	?	?
Beaver 2012	•	•	?	?		?	?	•	•	?	•
Beaver 2017	•	•	?	?		?	?	•	•	?	?
Brown 2002	•	?		?			?		•	?	?
D'Cruz 2016	•	•	?		•			•		•	?
Damude 2016	•	•	?	?		?	?	•	•	?	?
Davis 2013	•	•		?			?		•	?	?
Emery 2016	•	•	?	?		?	?	•	•	•	?
Gambazzi 2018	•	•	?			?		•		?	?
GILDA 2016	•	•	?	?	•	?	?	•	•	•	?
GIVIO 1994	•	•	?	?	•	?	?	?	?	?	?
Grunfeld 1996	•	•	?	?		?	?	•	•	?	?
Grunfeld 2006	•	•	?	?		•	?	•	•	•	?
Grunfeld 2011	•	•		?			?		•	?	?



Figure 3. (Continued)

Grunfeld 2011	•	•		?			?		•	?	?
Hershman 2013	•	•		•			•		•	?	?
Jefford 2016	•	?		?		?	?		•	•	?
Jeppesen 2018	•	•		?			?		•	•	?
Juarez 2013	?	?		?			?		•	?	•
Kimman 2011	•	•		?			?		•	•	?
Kirshbaum 2017	?	?		?			?		?	?	?
Kjeldsen 1997	?	?	?	?	•	?	?	•	•	?	?
Koinberg 2004	•	•	?	?	•	?	?	•	•	?	?
Kokko 2003	?	?	?		•	?		•		?	?
Kvale 2016	•	?		?			?		•	?	?
Mäkelä 1992	?	?	?		•	?		•		?	?
Malmstrom 2016	•	•		?			?		•	?	?
Maly 2017	•	•		?		?			•	?	?
Monteil 2010	?	?	?		•	?		?		•	?
Morrison 2018	•	•		?			?		•	•	?
Murchie 2010	•	•		?			?	•	•	?	•
Ohlsson 1995	?	?	?		•	?		•		?	?
Oltra 2007	?	?	?			?		•		?	?
Picardi 2014	•	•	?			?		•		?	?
Pietra 1998	?	?	?		•	?		•		?	?
Primrose 2014	•	•	?		•	?		•		?	?
Rodríguez-Moranta 2006	•	•	?		•	?		•		?	?
ROGY 2015	•	•		•			•		•	•	?
Rosselli Del Turco 1994	•	•	?		•	?		?		?	?
Ruddy 2016	?	?	?	?			?	•	•	•	•
Rustin 2007	•	•	?			?		•		•	?
Schoemaker 1998	•	•	?		•			•		?	?
Secco 2002	?	?	?		•	?		?		?	?
Sheppard 2009	•	•	?	?		?	?	?	?	?	?
Sobhani 2008	?	?	?			?		•		?	?
	-	•						•		. '	. '



Figure 3. (Continued)



#### Allocation

### Random sequence generation

Forty studies clearly stated the methods used for random sequence generation and we judged the risk of selection bias in these studies to be low (Augestad 2013; Beaver 2009; Beaver 2012; Beaver 2017; Brown 2002; D'Cruz 2016; Damude 2016; Davis 2013; Emery 2016; Gambazzi 2018; GILDA 2016; GIVIO 1994; Grunfeld 1996; Grunfeld 2006; Grunfeld 2011; Hershman 2013; Jefford 2016; Jeppesen 2018; Kimman 2011; Koinberg 2004; Kvale 2016; Malmstrom 2016; Maly 2017; Morrison 2018; Murchie 2010; Picardi 2014; Primrose 2014; Rodríguez-Moranta 2006; ROGY 2015; Rosselli Del Turco 1994; Rustin 2007; Schoemaker 1998; Sheppard 2009; Sobhani 2018; Van der Meulen 2013; Verschuur 2009; Wattchow 2006; Westeel 2012; Wille-Jorgensen 2018; Young 2013). The remaining thirteen studies did not provide sufficient information and we judged the risk of bias to be unclear (Juarez 2013; Kirshbaum 2017; Kjeldsen 1997; Kokko 2003; Mäkelä 1992; Monteil 2010; Ohlsson 1995; Oltra 2007; Pietra 1998; Ruddy 2016; Secco 2002; Sobhani 2008; Wang 2009.

#### Allocation concealment

We judged 37 studies to be at low risk of bias (Augestad 2013; Beaver 2009; Beaver 2012; Beaver 2017; D'Cruz 2016; Damude 2016; Davis 2013; Emery 2016; Gambazzi 2018; GILDA 2016; GIVIO 1994; Grunfeld 1996; Grunfeld 2006; Grunfeld 2011; Hershman 2013; Jeppesen 2018; Kimman 2011; Koinberg 2004; Malmstrom 2016; Maly 2017; Morrison 2018; Murchie 2010; Picardi 2014; Primrose 2014; Rodríguez-Moranta 2006; ROGY 2015; Rosselli Del Turco 1994; Rustin 2007; Sheppard 2009; Sobhani 2018; Van der Meulen 2013; Verschuur 2009; Wang 2009; Wattchow 2006; Westeel 2012; Wille-Jorgensen 2018; Young 2013). We judged studies that reported using a telephone-, computer- or web-based method of allocation to be at low risk of bias even if they did not specifically report that the allocation was concealed from the personnel involved in assigning participants to the treatment arms. Fifteen studies did not provide sufficient information for us to clearly judge whether allocation was adequately concealed prior to assignment (Brown 2002; Jefford 2016; Juarez 2013; Kirshbaum 2017; Kjeldsen 1997; Kokko 2003; Kvale 2016; Mäkelä 1992; Monteil 2010; Ohlsson 1995; Oltra 2007; Pietra 1998; Ruddy 2016; Secco 2002; Sobhani 2008). We judged one study to be at high risk of selection bias (Schoemaker 1998), as participants were reported to be allocated by the assigner, "choosing the next card from a box of cards indicating the type of follow-up".

#### **Blinding**

Given the nature of this type of intervention, it is usually not possible to blind participants and personnel to intervention arms. Following recommendations from the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2017), we assessed the domains of performance bias and detection bias by outcome group: objective outcomes (survival, recurrence and costs) and patient-reported outcomes (health-related quality of life, depression and anxiety).

# Blinding of participants and personnel (performance bias)

Performance bias refers to systematic differences between groups in the care that is provided or received and requested (Higgins 2017). We judged all studies that reported on the objective outcomes of survival and time to detection of recurrence to be at unclear risk of bias, as blinding was either not possible or not done. All the studies reporting on patient-reported outcomes we judged to be at unclear risk of bias except three, which we judged to be at low risk of bias, as these three studies reported that participants were blinded (Hershman 2013; ROGY 2015; Van der Meulen 2013).

# Blinding of outcome assessment (detection bias)

Detection bias refers to systematic differences between groups in how outcomes are determined (Higgins 2017). Here, we assessed the risk separately for the objective outcomes of survival and time to detection of recurrence. Since there can be no doubt whether a person is dead or alive, we judged all the studies reporting on overall survival to be at low risk of bias with regards to this outcome (GILDA 2016; GIVIO 1994; Kjeldsen 1997; Koinberg 2004; Kokko 2003; Mäkelä 1992; Monteil 2010; Ohlsson 1995; Pietra 1998; Primrose 2014; Rodríguez-Moranta 2006; Rosselli Del Turco 1994; Schoemaker 1998; Secco 2002; Sobhani 2018; Wang 2009; Wattchow 2006; Westeel 2012; Wille-Jorgensen 2018). With regards to time to detection of recurrence, we judged the risk to be unclear,



as we cannot rule out the possibility that the lack of blinding may influence judgement regarding clinical tests and assessments, which might influence the outcome. However, one study (Grunfeld 2006), reported that, "the outcome was assessed by a committee that was blinded to treatment allocation" so we judged it as low risk of detection bias for this outcome. With regards to patient-reported outcomes, all of which were collected through self-reported questionnaires, we judged all the studies, except the three mentioned above (Hershman 2013; ROGY 2015; Van der Meulen 2013), to be at unclear risk because participants were self-assessors and were not blinded.

#### Incomplete outcome data

Attrition bias refers to systematic differences between groups in withdrawals from a study (Higgins 2017). Following recommendations from the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2017), we assessed the domain of attrition bias by outcome group as the same study may have low risk of bias for objective outcomes (where information on death or recurrence is available from hospital records) but a high risk of bias for patient-reported outcomes (due to unreturned questionnaires).

Studies reporting on objective outcomes where missing outcome data were balanced and due to similar reasons in both groups, we judged to be at low risk of bias (Augestad 2013; Beaver 2012; Beaver 2017; D'Cruz 2016; Damude 2016; Emery 2016; Gambazzi 2018; GILDA 2016; Grunfeld 1996; Grunfeld 2006; Kimman 2011; Kjeldsen 1997; Koinberg 2004; Kokko 2003; Mäkelä 1992; Murchie 2010; Ohlsson 1995; Oltra 2007; Picardi 2014; Pietra 1998; Primrose 2014; Rodríguez-Moranta 2006; Ruddy 2016; Rustin 2007; Schoemaker 1998; Sobhani 2008; Sobhani 2018; Verschuur 2009; Wang 2009; Wattchow 2006; Westeel 2012; Wille-Jorgensen 2018). Five studies did not report reasons for dropout and we judged them to be at unclear risk of bias (GIVIO 1994; Monteil 2010; Rosselli Del Turco 1994; Secco 2002; Sheppard 2009). We judged one study (Beaver 2009), to be at high risk of bias, as more participants in the intervention group did not receive the intervention or wanted to change group and were lost to follow-up compared to the comparison group.

We judged studies reporting on patient-reported outcomes, where response rates were balanced and missing data were due to similar reasons in both groups, to be at low risk of bias (Augestad 2013; Beaver 2017; Brown 2002; Damude 2016; Davis 2013; Emery 2016; GILDA 2016; Grunfeld 1996; Grunfeld 2006; Grunfeld 2011; Hershman 2013; Jefford 2016; Jeppesen 2018; Kimman 2011; Kjeldsen 1997; Koinberg 2004; Kvale 2016; Malmstrom 2016; Maly 2017; Morrison 2018; Murchie 2010; Ruddy 2016; Van der Meulen 2013; Verschuur 2009; Wattchow 2006; Young 2013). Three studies insufficiently reported reasons for loss to follow-up or information on whether attrition was equally distributed between the groups, and we judged the risk of bias to be unclear (GIVIO 1994; Kirshbaum 2017; Sheppard 2009). We judged four studies to be at high risk of bias due to high attrition, imbalance in numbers or different reasons for attrition between the two groups (Beaver 2009; Beaver 2012; Juarez 2013; ROGY 2015).

# Selective reporting

Sixteen studies had available study protocols or prospectively registered clinical trial entries where all of the studies' prespecified outcomes had been reported and we judged these studies to be at low risk of reporting bias (Augestad 2013; D'Cruz 2016; Emery

2016; GILDA 2016; Grunfeld 2006; Jefford 2016; Jeppesen 2018; Kimman 2011; Monteil 2010; Morrison 2018; ROGY 2015; Rustin 2007; Sobhani 2018; Westeel 2012; Wille-Jorgensen 2018; Young 2013). We judged one study (Ruddy 2016), as being at high risk of reporting bias, as they did not report results for anxiety and depression in the publication, even though it was an outcome that was specified in the methods section. The remaining studies received a judgement of unclear risk, either because no study protocol was available for these studies or because they did not report all the outcomes specified in the protocol.

### Other potential sources of bias

We judged four studies to be at high risk of bias due to the potential risk of contamination, the risk of surveillance bias, significant baseline imbalances, or a combination of two or all of these (Beaver 2012; Juarez 2013; Murchie 2010; Ruddy 2016). Four other studies also reported baseline imbalances but we had difficulty identifying whether the imbalance would introduce bias and thus, judged them to be at unclear risk: Grunfeld 1996 had more stage I participants in the hospital group compared to the GP group (50.3% versus 40.4%); Ohlsson 1995 had fewer women and more men in the control group compared to the intervention group (23 versus 33 women, 31 versus 20 men); Oltra 2007 had more disease stage I participants in the intervention group (28 versus 17) and more stage IIA participants in the comparison group (24 versus 11); and Secco 2002 had more participants with higher levels of pre-operative carcinoembryonic antigen (CEA) and fewer participants with lower levels of pre-operative CEA in the intervention group compared to the comparison group (31.5% versus 9.5%, 68.5% versus 90.5%). Kirshbaum 2017 did not record any baseline information other than age of the participants and we also judged the risk to be unclear. We judged the remaining studies to be at unclear risk of other bias.

# **Effects of interventions**

See: Summary of findings for the main comparison Nonspecialist-led versus specialist-led follow-up after primary cancer treatment; Summary of findings 2 Less intensive versus more intensive follow-up after primary cancer treatment; Summary of findings 3 Follow-up integrating additional patient symptom education or monitoring, or survivorship care plans versus usual care

Below, we present the effects of the interventions by outcome for each comparison group. For each outcome, we present the results of the meta-analyses, the meta-regression and sensitivity analyses for overall survival and time to detection of recurrence (if carried out) and a narrative synthesis of the studies with results that we could not pool.

#### Comparison 1: non-specialist-led versus specialist-led followup

We included 17 studies for this comparison (Augestad 2013; Beaver 2009; Beaver 2012; Beaver 2017; Brown 2002; Emery 2016; Grunfeld 1996; Grunfeld 2006; Jeppesen 2018; Kimman 2011; Kirshbaum 2017; Koinberg 2004; Morrison 2018; Murchie 2010; Sheppard 2009; Verschuur 2009; Wattchow 2006).

# Overall survival

Four studies reported on the outcome of survival (Grunfeld 2006; Koinberg 2004; Verschuur 2009; Wattchow 2006).



Two studies reported data that we could pool in a meta-analysis investigating nurse-led follow-up after breast cancer (Koinberg 2004), and GP-led follow-up after colon cancer (Wattchow 2006). It is uncertain how non-specialist-led follow-up affects overall survival as the certainty of the evidence is very low (HR 1.21, 95% CI 0.68 to 2.15; P = 0.07; 2 studies; 603 participants; Analysis 1.1; Figure 4). The anticipated absolute effect was 2 fewer survivors per 100

patients (ranging from 10 fewer to 4 more). There was no statistical heterogeneity ( $I^2=0$ ) and we could not carry out meta-regression or sensitivity analyses. We downgraded the certainty of evidence by three levels for very serious concerns regarding indirectness and imprecision, as representativeness is limited with only two studies, the HRs were not reported but indirectly estimated and the confidence interval was very wide.

Figure 4. Forest plot of comparison 1. Non-specialist-led versus specialist-led follow-up, outcome: 1.1 overall survival A HR greater than 1 indicates a higher hazard of death (worse survival) in the non-specialist arm and a lower hazard of death (better survival) in the specialist-led arm

			Hazard Ratio								
Study or Subgroup	log[Hazard Ratio]	SE	Weight	IV, Random, 95% CI			IV, Ra	ndom, 95%	6 CI		
Koinberg 2004	0.1989	0.38	59.4%	1.22 [0.58, 2.57]			_				
Wattchow 2006	0.1823	0.46	40.6%	1.20 [0.49, 2.96]				-			
Total (95% CI)			100.0%	1.21 [0.68, 2.15]			-		_		
Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.00, df = 1 (P = 0.98); $I^2$ = 0% Test for overall effect: Z = 0.66 (P = 0.51)							0.5 non-specia	list Favou	2 Irs speci	5 ialist-led	10

The remaining two studies (1077 participants) reported little or no difference in survival for GP-led follow-up after breast cancer (risk difference 0.18%, 95% CI -2.90 to 3.26; Grunfeld 2006) or nurse-led follow-up after oesophageal cancer ("7 died in each group"; P = 0.41; Verschuur 2009).

#### Time to detection of recurrence

Four studies reported on time to detection of recurrence (Beaver 2017; Grunfeld 2006; Koinberg 2004; Wattchow 2006), but we could not use the reported data to indirectly estimate HRs and we could not pool the results. Thus, it is uncertain how non-specialist-led follow-up affects time to detection of recurrence

Three studies (1435 participants) reported little or no difference in time to detection of recurrence for: GP-led follow-up after breast cancer (risk difference 2.02%, 95% CI –2.13 to 6.16; Grunfeld 2006); GP-led follow-up after colon cancer (log-rank P = 0.76; Wattchow 2006); and nurse-led follow-up after breast cancer (risk difference –0.3%, 95% CI –10 to 9; Koinberg 2004). The final study (Beaver 2017; 259 participants), investigated follow-up after endometrial cancer and reported median time to recurrence in the nurse-led arm (307 days; range 48 to 662) versus the hospital arm (172 days; range 99 to 436) but did not carry out any statistical analysis. We judged the certainty of evidence to be very low and downgraded by three levels for serious concerns regarding inconsistency, indirectness and imprecision due to few studies, reporting of results by different estimates that could not be pooled and high variance of the result estimates.

### Health-related quality of life

Thirteen studies reported on health-related quality of life using a variety of measurement scales and with varying follow-up periods (Augestad 2013; Beaver 2017; Brown 2002; Grunfeld 1996; Grunfeld 2006; Kimman 2011; Kirshbaum 2017; Maly 2017; Morrison 2018; Murchie 2010; Sheppard 2009; Verschuur 2009; Wattchow 2006). We present results below, according to measurement scale.

#### The Medical Outcomes Study Short Form Health Survey (SF-36)

The SF-36 (Ware 1994), is a 36-item self-reported questionnaire consisting of eight subscales (physical functioning, physical role

functioning, bodily pain, general health, vitality, social functioning, emotional role functioning and mental health) that can be grouped into two dimensions: the Physical Component Summary (PCS) and the Mental Component Summary (MCS). All scales have transformed scores from 0-100, with higher scores indicating better health. The MCID for the SF-36 has been estimated to be approximately five points (Wyrwich 2005).

Three studies (1406 participants) used the SF-36 (Grunfeld 1996; Grunfeld 2006; Murchie 2010). We were unable to pool the data for meta-analysis as the three studies did not report on the same subscales at 12 months of follow-up (criteria prespecified in the Data synthesis section). However, all three studies reported that non-specialist-led follow-up may make little or no difference to health-related quality of life. Two studies (1264 participants) investigated GP-led follow-up after breast cancer. Grunfeld 1996 reported small differences between groups in mean change scores from baseline to trial end at 18 months' follow-up for social functioning (-1.8, 95% CI -7.2 to 3.5), mental health (0.5, 95% CI -4.1 to 5.1) and general health (0.6, 95% CI -3.6 to 4.8). Grunfeld 2006 reported a figure showing similar mean scores between groups over time for SF-36 MCS and PCS with up to 60 months' follow-up. Murchie 2010 reported little or no effect of GP-led follow-up after melanoma on SF-36 scores for all subscales at 12 months' follow-up with P values ranging from P = 0.149 to P = 1.000 (142 participants).

# European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC-C30)

The EORTC-C30 is a 30-item, self-reported questionnaire consisting of six subscales (physical functioning, role functioning, social functioning, emotional functioning, cognitive functioning and global health status) and other single items on symptoms (Aaronson 1993). All scales have scores from 0 to 100, with higher scores indicating better health. The MCID for the EORTC-C30 has been estimated to be approximately 10 points (Osoba 1998).

Seven studies reported on quality of life using the EORTC-C30 (Augestad 2013; Beaver 2017; Brown 2002; Kimman 2011; Kirshbaum 2017; Morrison 2018; Verschuur 2009). We were able to pool data from four studies investigating GP-led follow-up after colon cancer (Augestad 2013), nurse-led follow-up after



breast cancer (Kimman 2011), patient-initiated follow-up after breast cancer (Kirshbaum 2017), and nurse-led follow-up after oesophageal cancer (Verschuur 2009). We carried out metaanalyses for all six subscales, although Kimman 2011 did not report data for the subscales physical functioning, cognitive functioning and social functioning. Compared to specialist-led follow-up, nonspecialist-led follow-up may make little or no difference at 12 months to: global health status (MD 1.06, 95% CI -1.83 to 3.95; P = 0.47,  $I^2 = 32\%$ ; 4 studies, 605 participants; Analysis 1.2); physical functioning (MD 1.65, 95% CI -2.35 to 5.64; P = 0.42, I<sup>2</sup> = 47%; 3 studies, 306 participants; Analysis 1.3); role functioning (MD 2.36, 95% CI -2.75 to 7.47; P = 0.36, I<sup>2</sup> = 48%; 4 studies; participants = 605; Analysis 1.4); emotional functioning (MD 0.52, 95% CI -2.06 to 3.09; P = 0.69,  $I^2 = 0\%$ ; 4 studies, 605 participants; Analysis 1.5); and cognitive functioning (MD 4.41, 95% CI -1.52 to 10.34; P = 0.14, I<sup>2</sup> = 54%; 3 studies, 306 participants; Analysis 1.6). However, nonspecialist-led follow-up may slightly improve social functioning (MD 5.39, 95% CI 1.60 to 9.17; P = 0.005;  $I^2 = 0\%$ ; 3 studies, 306 participants; Analysis 1.7), but this difference was not large enough to be clinically meaningful. We judged the certainty of evidence to be low and downgraded by two levels for serious concerns regarding inconsistency and imprecision due to differing estimates of effect and wide confidence intervals.

Of the remaining three studies, two studies (320 participants) did not contradict the results of the meta-analyses. Beaver 2017 reported little or no effect of nurse-led telephone follow-up after endometrial cancer on all six subscales at time points ranging from 3 to 12 months after baseline data collection, and Brown 2002 investigated patient-initiated follow-up after breast cancer and reported similar median scores between groups on all subscales after 12 months of follow-up. The third study (Morrison 2018; 24 participants), reported improved health-related quality of life for nurse-led telephone follow-up after gynaecological cancer at six months for global health (MD 4.2, no 95% CI), physical functioning (MD 14.3, no 95% CI) and emotional functioning (MD 1.6, no 95% CI).

## Other measures of health-related quality of life

Four studies also reported that non-specialist-led follow-up made little or no difference to health-related quality of life using other measures than the above (659 participants). Wattchow 2006 reported on health-related quality of life using the 12-item Short Form Health Survey (SF-12; Ware 1995), and reported little or no effect of GP-led follow-up after colon cancer on the median scores for both subscales at 12 months (PCS, P = 0.887; MCS, P = 0.510). Two studies reported on health-related quality of life using the EuroQol-5D (EuroQoL 1990). Augestad 2013 reported little or no effect of GP-led follow-up after colon cancer in mean differences from baseline to 24 months (P = 0.48) and Verschuur 2009 reported little or no effect of nurse-led follow-up after oesophageal cancer on mean scores at 13 months (P = 0.58). Using the Functional Assessment of Cancer Therapy (FACT) scale, Sheppard 2009 reported little or no effect of nurse-led patientinitiated follow-up after breast cancer on mean scores at 18 months of follow-up (P = 0.952).

# Anxiety

Twelve studies reported on the outcome of anxiety using a variety of measurement scales and with varying follow-up periods (Beaver 2009; Beaver 2012; Beaver 2017; Brown 2002; Emery 2016; Grunfeld 1996; Grunfeld 2006; Kimman 2011; Kirshbaum 2017; Koinberg

2004; Murchie 2010; Wattchow 2006), and two studies reported on fear of recurrence (Jeppesen 2018; Sheppard 2009). We present below results according to measurement scale.

## State Trait Anxiety Inventory (STAI) - state subscale

The STAI is a 40-item, self-reported questionnaire consisting of two subscales (state anxiety and trait anxiety; Spielberger 1983). Subscales have scores ranging from 20 to 80, with higher scores indicating greater anxiety. The MCID for the STAI has been estimated to be approximately 10 points (Corsaletti 2014).

Four studies reported on state anxiety using STAI (Beaver 2009; Beaver 2012; Beaver 2017; Kimman 2011), and three reported data that we could pool in a meta-analysis (Beaver 2009; Beaver 2012; Kimman 2011). Compared to specialist-led follow-up, non-specialist-led follow-up may make little or no difference to anxiety at 12 months' follow-up as measured by STAI state subscale (MD –0.55, 95% CI –2.41 to 1.32; P = 0.57; I² = 0%; 3 studies, 602 participants; Analysis 1.8). We judged the certainty of evidence to be low as we downgraded by two levels for serious concerns regarding study limitations (high risk of attrition bias for two of the studies) and indirectness due to only three studies.

We did not include results from Beaver 2017 in the meta-analysis as the reported final scores included follow-up periods of 3, 6 and 12 months (259 participants). However, the study reported the non-inferiority of nurse-led follow-up in endometrial cancer (MD 0.7, 95% CI -1.9 to 3.3).

#### Hospital Anxiety and Depression Scale (HADS)-Anxiety subscale

The HADS is a 14-item, self-reported questionnaire consisting of two subscales (anxiety and depression; Snaith 2003). Subscales have scores from 0 to 21, with higher scores indicating greater anxiety or depression. The MCID for the HADS has been estimated to be approximately 1.5 points (Puhan 2008).

Eight studies reported on anxiety using the HADS-Anxiety subscale (Brown 2002; Emery 2016; Grunfeld 1996; Grunfeld 2006; Kirshbaum 2017; Koinberg 2004; Murchie 2010; Wattchow 2006). Five studies contributed data to the meta-analysis investigating patient-initiated follow-up after breast cancer (Brown 2002), shared-care after prostate cancer (Emery 2016), GP-led followup after breast cancer (Grunfeld 2006), patient-initiated followup after breast cancer (Kirshbaum 2017), and GP-led follow-up after colon cancer (Wattchow 2006). Compared to specialist-led follow-up, non-specialist-led follow-up probably makes little or no difference to anxiety at 12 months' follow-up as measured by HADS-Anxiety subscale (MD -0.03, 95% CI -0.73 to 0.67; P = 0.94, I<sup>2</sup> = 51%; 5 studies, 1266 participants; Analysis 1.9). Sensitivity analysis (where we removed estimates that were indirectly derived from Brown 2002) did not change our conclusion (MD 0.27, 95% CI -0.15 to 0.69; P = 0.21; 4 studies, 1210 participants). We judged the certainty of evidence to be moderate as we downgraded by one level for concerns regarding inconsistency of results ( $I^2 = 51\%$ ) and indirectness due to few studies.

The remaining three studies did not contradict the results of the meta-analyses (702 participants). Grunfeld 1996 reported little or no effect of GP-led follow-up after breast cancer on mean change from baseline to the end of the study (MD 0.4, 95% CI –0.3 to 1.2). Koinberg 2004 and Murchie 2010 reported dichotomised results with little or no effect of nurse-led follow-up after breast cancer at



18 months (RR 1.2, 95% CI 0.4 to 3.1) and GP-led follow-up after melanoma at 12 months (P = 0.87) respectively.

#### Fear of recurrence

Two studies reported conflicting results on fear of recurrence. Jeppesen 2018 reported that fear of recurrence decreased more in the comparison group than in the patient-initiated group at 10 months' follow-up (MD -5.9, 95% CI -10.9 to -0.9; P = 0.02; 214 participants) as measured by the Fear of Cancer Recurrence Inventory (Simard 2009), while Sheppard 2009 reported little or no effect of nurse-led patient-initiated follow-up after breast cancer on fear of recurrence at 18-months (MD 0.5 95% CI -0.3 to 1.0; 237 participants) using a three-item questionnaire that was yet to be tested at that time.

#### Depression

Eleven studies reported on the outcome of depression or psychological distress using a variety of measurement scales and with varying follow-up periods (Beaver 2009; Beaver 2012; Brown 2002; Emery 2016; Grunfeld 1996; Grunfeld 2006; Kirshbaum 2017; Koinberg 2004; Murchie 2010; Sheppard 2009; Wattchow 2006). We present a synthesis according to measurement scale below:

#### Hospital Anxiety and Depression Scale (HADS)-Depression subscale

Eight studies reported on depression using the HADS-Depression subscale (Brown 2002; Emery 2016; Grunfeld 1996; Grunfeld 2006; Kirshbaum 2017; Koinberg 2004; Murchie 2010; Wattchow 2006). Five studies contributed data to the meta-analysis investigating patient-initiated follow-up after breast cancer (Brown 2002), shared-care after prostate cancer (Emery 2016), GP-led followup after breast cancer (Grunfeld 2006), patient-initiated followup after breast cancer (Kirshbaum 2017) and GP-led follow-up after colon cancer (Wattchow 2006). Compared to specialist-led follow-up, non-specialist-led follow-up makes little or no difference to depression at 12-months as measured by HADS-Depression subscale (MD 0.03, 95% CI -0.35 to 0.42; P = 0.86;  $I^2 = 8\%$ ; 5 studies, 1266 participants; Analysis 1.10). Sensitivity analysis (where we removed estimates that were indirectly derived from Brown 2002) did not change our conclusion (MD 0.19, 95% CI -0.18 to 0.56; P = 0.30; 4 studies, 1210 participants). We judged the certainty of evidence to be high although we had some concerns regarding indirectness due to few studies, but we did not judge it serious enough to warrant downgrading the evidence by a whole level.

The remaining three studies did not contradict the results of the meta-analyses (702 participants). Grunfeld 1996 reported little or no effect on depression for GP-led follow-up after breast cancer on mean change from baseline to the end of the trial (MD 0.4, 95% CI -0.2 to 1.1). Koinberg 2004 and Murchie 2010 reported little or no effect on depression for nurse-led follow-up after breast cancer at 18 months (RR 0.5, 95% CI 0.0 to 5.8) and GP-led follow-up after melanoma at 12 months (P = 0.91) respectively.

# Other measures of depression

The remaining three studies (676 participants) also reported that non-specialist-led follow-up may make little or no difference to depression. The studies reported using the General Heath Questionnaire (GHQ-12; Goldberg 1978). Beaver 2009 reported that, "Although the percentage of cases (scores ≥4) was consistently higher in the hospital group at the start, middle, and end of the trial, differences between the groups at each time point were not

significant". Beaver 2012 reported that mean GHQ-12 score was slightly higher in the hospital arm (Cohen's d = 0.11), and Sheppard 2009 reported little or no differences between the point-of-need (patient-initiated) and routine follow-up (MD 0.1, 95% CI -1.4 to 1.0, P = 0.767).

#### Cost

Eight studies reported cost outcomes (Augestad 2013; Beaver 2009; Beaver 2017; Grunfeld 1996; Kimman 2011; Koinberg 2004; Morrison 2018; Verschuur 2009), but due to the substantial heterogeneity in how the outcome was measured and reported, we could not pool the results in a meta-analysis (1756 participants). Details of how each study measured and reported cost outcomes are summarised in Table 1. In general, Augestad 2013; Beaver 2017; Grunfeld 1996; Koinberg 2004; Morrison 2018; and Verschuur 2009 reported lower cost per participant in the non-specialist-led group, while Beaver 2009 and Kimman 2011 reported higher cost per participant in the non-specialist-led group. We judged the certainty of evidence to be very low and downgraded by three levels as the substantial heterogeneity led to serious concerns regarding inconsistency, indirectness and imprecision in the way cost was measured and reported across studies.

### Comparison 2: less intensive versus more intensive follow-up

We included 24 studies for this comparison (D'Cruz 2016; Damude 2016; Gambazzi 2018; GILDA 2016; GIVIO 1994; Kjeldsen 1997; Kokko 2003; Mäkelä 1992; Monteil 2010; Ohlsson 1995; Oltra 2007; Picardi 2014; Pietra 1998; Primrose 2014; Rodríguez-Moranta 2006; Rosselli Del Turco 1994; Rustin 2007; Schoemaker 1998; Secco 2002; Sobhani 2008; Sobhani 2018; Wang 2009; Westeel 2012; Wille-Jorgensen 2018).

#### Overall survival

Eighteen studies reported on the outcome of survival (D'Cruz 2016; GILDA 2016; GIVIO 1994; Kjeldsen 1997; Kokko 2003; Mäkelä 1992; Monteil 2010; Ohlsson 1995; Pietra 1998; Primrose 2014; Rodríguez-Moranta 2006; Rosselli Del Turco 1994; Schoemaker 1998; Secco 2002; Sobhani 2018; Wang 2009; Westeel 2012; Wille-Jorgensen 2018).

Thirteen studies reported data that we could pool for meta-analysis investigating less versus more intensive follow-up after oral cancer (D'Cruz 2016), breast cancer (GIVIO 1994; Rosselli Del Turco 1994), non-small cell lung cancer (Westeel 2012), and colorectal cancer (GILDA 2016; Kjeldsen 1997; Mäkelä 1992; Ohlsson 1995; Rodríguez-Moranta 2006; Schoemaker 1998; Sobhani 2018; Wang 2009; Wille-Jorgensen 2018).

Compared to more intensive follow-up, we found that less intensive follow-up may make little or no difference to overall survival (HR 1.05, 95% CI 0.96 to 1.14; P = 0.29, I² = 8%; 13 studies, 10,726 participants; Analysis 2.1; Figure 5). The anticipated absolute effect was 1 fewer survivor per 100 patients (ranging from 3 fewer to 1 more). A funnel plot showed no detectable publication bias. We judged the certainty of evidence to be low as we downgraded by two levels for some concerns regarding study limitations (lack of allocation concealment in one study, Schoemaker 1998) and indirectness as the studies were primarily investigating follow-up after colorectal and breast cancer, and serious concerns regarding imprecision as the confidence interval includes effects that are not trivial (potentially up to 3 fewer survivors per 100 patients).



Sensitivity analysis (where we removed estimates that were indirectly derived from the following studies Kjeldsen 1997; Mäkelä 1992; Ohlsson 1995; Rosselli Del Turco 1994; Sobhani 2018), gave a

similar result (HR 1.07, 95% CI 0.96 to 1.19; P = 0.24; 8 studies, 9037 participants).

Figure 5. Forest plot of comparison 2. Less intensive versus more intensive follow-up, outcome: 2.1 overall survival A HR greater than 1 indicates a higher hazard of death (worse survival) in the less intensive arm and a lower hazard of death (better survival) in more intensive arm

				Hazard Ratio	Hazard Ratio
Study or Subgroup	log[Hazard Ratio]	SE	Weight	IV, Random, 95% CI	I IV, Random, 95% CI
D'Cruz 2016	0.207	0.24	3.2%	1.23 [0.77, 1.97]	·]
GILDA 2016	-0.1312	0.14	8.8%	0.88 [0.67, 1.15]	i) <del> </del>
GIVIO 1994	-0.1054	0.13	10.0%	0.90 [0.70, 1.16]	·i] ————————————————————————————————————
Kjeldsen 1997	0.1044	0.15	7.7%	1.11 [0.83, 1.49]	ıj <del> -</del>
Mäkelä 1992	0.1906	0.28	2.4%	1.21 [0.70, 2.09]	ıj — — — — — — — — — — — — — — — — — — —
Ohlsson 1995	0.3709	0.33	1.7%	1.45 [0.76, 2.77]	7]
Rodríguez-Moranta 2006	0.1392	0.29	2.2%	1.15 [0.65, 2.03]	nj — <del> </del>
Rosselli Del Turco 1994	-0.0513	0.09	18.8%	0.95 [0.80, 1.13]	·] —
Schoemaker 1998	0.371	0.2	4.5%	1.45 [0.98, 2.14]	·]
Sobhani 2018	-0.6255	0.45	0.9%	0.53 [0.22, 1.29]	ıj <del></del>
Wang 2009	0.3436	0.22	3.8%	1.41 [0.92, 2.17]	'1 <del>  •</del>
Westeel 2012	0.0513	0.08	22.6%	1.05 [0.90, 1.23]	·] ————————————————————————————————————
Wille-Jorgensen 2018	0.1044	0.11	13.4%	1.11 [0.89, 1.38]	·1 +
Total (95% CI)			100.0%	1.05 [0.96, 1.14]	ı <b>•</b>
Heterogeneity: Tau² = 0.00; Test for overall effect: Z = 1		2 (P = I	0.1 0.2 0.5 1 2 5 10 Favours less intensive Favours more intensive		

We carried out meta-regression analysis to quantify clinical heterogeneity and found little or no difference in the intervention effect by cancer site (breast, colorectal, lung, oral), P = 0.32; year of publication (before 2000, from 2000 onwards), P = 0.87; or study quality (high, moderate, low), P = 0.71. We did not carry out meta-regression for participant age or sex, as age was similar across studies (approximately 60 to 65 years) and sex was either associated with cancer site (e.g. breast cancer) or effects were not reported separately by sex in studies with both men and women.

We could not incorporate data from five other studies (Kokko 2003; Monteil 2010; Pietra 1998; Primrose 2014; Secco 2002). Three of these studies (1752 participants) reported no difference between less and more intensive follow-up on overall survival after breast cancer (five-year survival rate = 85% versus 85%, no P-value; Kokko 2003), lung cancer ("overall survival" = 26,5 months  $\pm$  19.6 versus 29 months  $\pm$  17.1, no P-value; Monteil 2010), and colorectal cancer (survival curves comparing all four arms, log-rank P = 0.56; Primrose 2014). The remaining two studies (544 participants) reported improved survival outcomes with more intensive follow-up after colorectal cancer. Pietra 1998 reported improved cumulative survival rates (73% versus 58%, log-rank P < 0.02) and Secco 2002 reported improved actuarial five-year survival rates (for high-risk patients: Chi² = 4.97, P < 0.05 and for low-risk patients: Chi² = 7.90, P < 0.01).

#### Time to detection of recurrence

Twenty-two studies reported on time to detection of recurrence (Damude 2016; Gambazzi 2018; GILDA 2016; GIVIO 1994; Kjeldsen

1997; Kokko 2003; Mäkelä 1992; Monteil 2010; Ohlsson 1995; Oltra 2007; Picardi 2014; Pietra 1998; Primrose 2014; Rodríguez-Moranta 2006; Rosselli Del Turco 1994; Rustin 2007; Secco 2002; Sobhani 2008; Sobhani 2018; Wang 2009; Westeel 2012; Wille-Jorgensen 2018).

Twelve studies reported data that we were able to pool for metaanalysis investigating less versus more intensive follow-up after colorectal cancer (GILDA 2016; Kjeldsen 1997; Primrose 2014; Rodríguez-Moranta 2006; Sobhani 2008; Wille-Jorgensen 2018), breast cancer (GIVIO 1994; Rosselli Del Turco 1994), non-small cell lung cancer (Gambazzi 2018; Westeel 2012), Hodgkin lymphoma (Picardi 2014) and testicular cancer (Rustin 2007).

Compared to more intensive follow-up, less intensive follow-up probably increases time to detection of recurrence (HR 0.85, 95% CI 0.79 to 0.92; P < 0.0001, I<sup>2</sup> = 0; 12 studies, 11,276 participants; Analysis 2.2, Figure 6). The anticipated absolute effect was 3 fewer detected recurrences per 100 patients (ranging between 5 to 2 fewer). A funnel plot showed no detectable publication bias. We judged the certainty of evidence to be moderate as we downgraded by one level for serious concerns regarding indirectness as HRs for eight of the studies were not reported but indirectly estimated from published data. Sensitivity analysis (where we removed all the studies except GILDA 2016; Picardi 2014; Westeel 2012; Wille-Jorgensen 2018), showed that less intensive follow-up may still delay detection of recurrence (HR 0.87, 95% CI 0.79 to 0.96; P = 0.006; 4 studies, 5872 participants).



Figure 6. Forest plot of comparison 2. Less intensive versus more intensive follow-up, outcome: 2.2 time-to-detection of recurrence A HR less than 1 indicates a lower hazard of detecting recurrence (delay in detection of recurrence) in the less intensive arm and a higher hazard of detecting recurrence (better detection of recurrence) in the more intensive arm.

				Hazard Ratio	Hazard Ratio
Study or Subgroup	log[Hazard Ratio]	SE	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Gambazzi 2018	0.2359	0.38	1.0%	1.27 [0.60, 2.67]	
GILDA 2016	-0.1989	0.13	8.2%	0.82 [0.64, 1.06]	<del></del>
GIVIO 1994	-0.1485	0.13	8.2%	0.86 [0.67, 1.11]	<del></del>
Kjeldsen 1997	0.0411	0.16	5.4%	1.04 [0.76, 1.43]	<del></del>
Picardi 2014	0.0266	0.2299	2.6%	1.03 [0.65, 1.61]	<del></del>
Primrose 2014	-0.3159	0.1231	9.1%	0.73 [0.57, 0.93]	
Rodríguez-Moranta 2006	-0.0587	0.24	2.4%	0.94 [0.59, 1.51]	<del></del>
Rosselli Del Turco 1994	-0.2627	0.1	13.8%	0.77 [0.63, 0.94]	
Rustin 2007	-0.3011	0.24	2.4%	0.74 [0.46, 1.18]	<del></del>
Sobhani 2008	-0.1744	0.29	1.6%	0.84 [0.48, 1.48]	<del></del>
Westeel 2012	-0.131	0.07	28.2%	0.88 [0.76, 1.01]	
Wille-Jorgensen 2018	-0.1397	0.09	17.1%	0.87 [0.73, 1.04]	
Total (95% CI)			100.0%	0.85 [0.79, 0.92]	<b>♦</b>
Heterogeneity: Tau² = 0.00;	Chi² = 6.83, df = 11	(P = 0.81)	); I <sup>2</sup> = 0%		01 02 05 1 2 5 10
Test for overall effect: Z = 4	.32 (P < 0.0001)				0.1 0.2 0.5 1 2 5 10 Favours more intensive Favours less intensive
					ravours more intensive. Lavours less intensive

We carried out meta-regression analysis to quantify clinical heterogeneity and found little or no difference in the intervention effect by cancer site (breast, colorectal, lung, other), P=0.81; year of publication (before 2000, from 2000 onwards), P=0.89 or study quality (high, moderate, low), P=0.42. We did not carry out meta-regression for participant age or sex, as age was similar across studies (approximately 60 to 65 years) and sex was either associated with cancer site (e.g. breast cancer) or effects were not reported separately by sex in studies with both men and women.

We could not incorporate data from 10 other studies (Damude 2016; Kokko 2003; Mäkelä 1992; Monteil 2010; Ohlsson 1995; Oltra 2007; Pietra 1998; Secco 2002; Sobhani 2018; Wang 2009). Four of these studies (854 participants) reported shorter time to detection of recurrence for more intensive follow-up after colorectal cancer (mean/SD  $10 \pm 5$  versus  $15 \pm 10$  months, P = 0.002; Mäkelä 1992 and mean/SD  $10.3 \pm 2.7$  versus  $20.2 \pm 6.1$  months, P < .0003; Pietra 1998), lung cancer (mean/SD  $12 \pm 9.9$  versus  $18 \pm 11.8$  months, no P-value; Monteil 2010) and breast cancer (mean 1.9 versus 2.1 years, no Pvalue; Kokko 2003). Four other studies (734 participants) reported little or no difference between groups on time to recurrence after melanoma (no estimate reported by the authors, only Chi<sup>2</sup> P-value = 0.893; Damude 2016), colorectal cancer (median 1.7 (range 0.3 to 7.6) years versus 2.0 (range 0.8 - 5.6) years, P > 0.05; Ohlsson 1995), (mean/SD 22  $\pm$  17.6 months versus 35  $\pm$  23.9 months, P = 0.49; Wang 2009), and detection of recurrence after breast cancer at three years' follow-up (22.41%, 90% CI 13.40 to 31.42 versus 17.46%, 90% CI 9.59 to 25.30; Oltra 2007). One final study, Secco 2002, also reported on "disease-free intervals" but the outcome data were not relevant for this review as the study compared high-risk patients with low-risk patients instead of patients in the intensive treatment group with patients in the minimal treatment group (337 participants). Finally, Sobhani 2018 only reported on detection of unresectable recurrence in colorectal cancer (7.0 versus 14.3 months in favour of the more intensive arm; 239 participants).

The delay in detection of recurrence between the two arms ranged from 2 to 10 months in the studies that reported the outcome in time. However, the clinical relevance of this delay on patient outcomes, such as survival, is uncertain as this depends on multiple

factors, such as cancer site, treatment received or the patient's disease burden, and the studies included were not designed to address this.

# Health-related quality of life

Three studies reported on health-related quality of life (Damude 2016; GILDA 2016; GIVIO 1994), but we could not pool the reported data due to the different measures used and varying follow-up periods. However, all three studies (2742 participants) reported that less intensive follow-up made little or no difference in healthrelated quality of life when compared to more intensive follow-up. Damude 2016 used the MCS subscale of the RAND-36 (a version of the SF-36) and reported that less intensive follow-up after melanoma had no effect on health-related quality of life at 12 months (mean/SD 54.3 (7.6) versus 52.5 (8.8); P = 0.62). GILDA 2016 used the SF-12 and reported graphs showing no difference between less intensive and more intensive follow-up after colorectal cancer on the PCS and MCS subscales of the SF-36 for up to 60 months of follow-up. GIVIO 1994 measured quality of life using a compilation of items selected from several quality-of-life instruments and reported that, "type of follow-up did not affect various dimensions of health-related quality of life" after breast cancer for up to five years' follow-up. We judged the certainty of evidence to be very low and downgraded by three levels for serious concerns regarding inconsistency, indirectness and imprecision due to the few studies, heterogeneous measures and reporting of results by different estimates that we could not pool.

#### Anxiety

Only Damude 2016 reported on anxiety using STAI and showed that less intensive follow-up after melanoma made little or no difference to anxiety at 12 months (mean/SD 29.5 (8.8) versus 31.0 (9.9); P = 0.54; 180 participants). We judged the certainty of evidence to be very low and downgraded by three levels for serious concerns regarding inconsistency, indirectness and imprecision since there was only one study.



#### Depression

None of the studies reported on depression. Thus, there is a lack of evidence for the effect of less intensive versus more intensive follow-up on depression following completion of primary cancer treatment in adult cancer survivors.

#### Cost

Six studies (1412 participants) reported cost outcomes (Damude 2016; Kokko 2003; Monteil 2010; Oltra 2007; Picardi 2014; Rodríguez-Moranta 2006), but due to the substantial heterogeneity in how studies measured and reported the outcome, we could not pool the results in a meta-analysis. We have summarised details of how each study measured and reported cost outcomes in Table 1. One study (Secco 2002) reported carrying out cost analysis but did not report any data. All studies reported lower costs for the less intensive arm from the perspective of the patient or healthcare system but the difference in cost varied considerably depending on the components of or procedures used in the different interventions. We judged the certainty of evidence to be very low and downgraded by three levels as the substantial heterogeneity led to serious concerns regarding inconsistency, indirectness and imprecision in the way cost was measured and reported across studies.

# Comparison 3: follow-up integrating additional patient symptom education or monitoring, or survivorship care plans versus usual care

We included 12 studies for this comparison (Davis 2013; Grunfeld 2011; Hershman 2013; Jefford 2016; Juarez 2013; Kvale 2016; Malmstrom 2016; Maly 2017; ROGY 2015; Ruddy 2016; Van der Meulen 2013; Young 2013).

# Overall survival

None of the studies reported on overall survival. Thus, there is a lack of evidence for the effect of follow-up integrating patient education/survivorship care plans versus usual care on survival following completion of primary cancer treatment in adult cancer survivors.

# Time to detection of recurrence

None of the studies reported on time to detection of recurrence. Thus, there is a lack of evidence for the effect of follow-up integrating patient education/survivorship care plans versus usual care on detection of recurrence following completion of primary cancer treatment in adult cancer survivors.

# Health-related quality of life

All twelve studies (2846 participants) reported on health-related quality of life using a variety of measurement scales and with varying follow-up periods. (Davis 2013; Grunfeld 2011; Hershman 2013; Jefford 2016; Juarez 2013; Kvale 2016; Malmstrom 2016; Maly 2017; ROGY 2015; Ruddy 2016; Van der Meulen 2013; Young 2013). We were unable to pool the reported data in a meta-analysis as there was no scale or subscale that at least three studies reported at 12 months of follow-up (criteria prespecified in the Data synthesis section). However, all the studies except Kvale 2016 reported little or no difference in health-related quality of life between the intervention and usual care groups. We present results below according to measurement scale.

Two studies used the SF-36. Grunfeld 2011 investigated a survivorship care plan intervention after breast cancer and unpublished results showed similar mean scores between groups at 12 months for both the PCS subscale (mean/SD 48.2 (8.8) versus 48.4 (9.4)) and MCS subscale (,mean/SD 51.4 (9.4) versus 49.5 (10.7)). Kvale 2016 investigated the POSTCARE intervention (survivorship care plan and patient coaching) after breast cancer and reported clinically meaningful improvement for physical role functioning (P = 0.009), bodily pain (P = 0.03) and emotional role functioning (P = 0.04) at three months' follow-up.

Three studies used the EORTC-C30. Jefford 2016 (the SurvivorCare intervention) and Malmstrom 2016 investigated the addition of patient supportive education or care packages to usual care after colorectal and oesophageal cancer respectively and both reported little or no difference on all subscales at six months between the intervention group and the usual care group. Unpublished results from ROGY 2015, investigating survivorship care plan after endometrial and ovarian cancer, also showed little or no difference on all subscales at 12 months between the survivorship care plan group and the usual care group.

Three studies used the SF-12. Davis 2013 investigated the addition of patient symptom education and monitoring after prostate cancer and reported, "no significant group differences at 7 months" (P > 0.10), Maly 2017 investigated the addition of treatment summaries and survivorship care plan after breast cancer and reported, "no significant differences in SF-12 scores from baseline to 12 months between groups (data not shown)", while Ruddy 2016 investigated a survivorship care plan with patient navigator intervention after breast cancer and reported similar medians and interquartile ranges in both groups at 12 months, but did not carry out any statistical analyses.

Three studies used various versions of the FACT scale. In addition to reporting on the SF-12 above, Davis 2013 also reported little or no effect as measured by FACT-G at seven months (P > 0.10). Young 2013 investigated the CONNECT intervention (additional patient education through structured telephone calls by trained nurses) after colorectal cancer and reported little or no effect as measured by the FACT-C at six months (P = 0.58), and Hershman 2013 investigated survivorship care plan with patient-nurse sessions after breast cancer and reported little or no effect as measured by the FACT-B at six months for the physical well-being subscale (P = 0.93) and functional well-being subscale (P = 0.83).

Juarez 2013 investigated an individualised bilingual patient education programme after breast cancer and used the City of Hope Quality of Life Questionnaire to measure quality of life at three and six months and reported that, "QoL [quality of life] increased slightly in both groups or remained unchanged, without significant group by time interaction."

Although all the studies but one reported consistent results, we judged the overall certainty of evidence to be very low and downgraded by three levels for serious concerns regarding study limitations, indirectness and imprecision due to studies being at high risk of bias, the heterogeneous measures and reporting of results by different estimates that could not be pooled.



#### Anxiety

Only ROGY 2015 reported on anxiety (470 participants). Unpublished data showed similar scores for both the survivorship care plan and usual care group on the HADS-Anxiety subscale at 12 months for endometrial cancer survivors (mean/SD 5 (4) versus 4.2 (3.6)) and ovarian cancer survivors (mean/SD 5.4 (3.9) versus 6.2 (4.5)). We judged the certainty of evidence to be very low and downgraded by three levels for serious concerns regarding inconsistency, indirectness and imprecision since there was only one study.

# Depression

Eight studies (2351 participants) reported on depression or psychological distress using a variety of measurement scales and with varying follow-up periods. (Grunfeld 2011; Hershman 2013; Jefford 2016; Juarez 2013; Kvale 2016; ROGY 2015; Van der Meulen 2013; Young 2013). We were unable to pool the reported data in a meta-analysis as there was no scale or subscale that at least three studies reported at 12 months of follow-up (criteria prespecified in the Data synthesis section). However, all the studies except Van der Meulen 2013 reported little or no difference in depression between the intervention and usual care groups. We present results below according to measurement scale.

One study used the HADS-Depression subscale. Unpublished results from ROGY 2015 showed similar mean scores for both the survivorship care plan and usual care groups at 12 months' follow-up among endometrial cancer survivors (mean/SD 3.8 (3.9) versus 3.7 (3.5)) and ovarian cancer survivors (mean/SD 3.5 (3.6) versus 4.4 (4.4)).

One study used the Profile of Mood States (POMS). Grunfeld 2011 reported little or no mean difference between the survivorship care plan and usual care groups at 12 months' follow-up among breast cancer survivors (MD 2.6, 95% CI 5.6 to 0.5).

One study used the Patient Health Questionnaine (PHQ-9). Kvale 2016 reported no difference between the POSTCARE and usual care groups in change scores from baseline to three-month follow-up among breast cancer survivors (P = 0.376).

One study used the Brief Symptom Inventory (BSI-18). Jefford 2016 reported little or no difference between the SurvivorCare and usual care groups at six months' follow-up among colorectal cancer survivors (MD -0.9, 95% CI -3.7 to 1.9).

Two studies each used the Center for Epidemiological Studies-Depression scale (CES-D). Hershman 2013 reported little or no difference between the survivorship care plan and usual care groups at six months' follow-up among breast cancer survivors (P = 0.83), while Van der Meulen 2013 reported a decrease in depressive symptoms in the 'NUCAI' survivorship care group compared with the usual care group at 12 months among head and neck cancer survivors (MD 2.8, 95% CI 5.2 to 0.3).

Two studies used the distress thermometer, a single-question screening instrument to evaluate patient's distress based on a scale of 1 to 10 during the past week. Both studies reported little or no difference between groups at six months among breast cancer and colorectal cancer survivors respectively: Juarez 2013 (P = 0.305) and Young 2013 (MD 0.3, 95% CI 0.8 to 0.2).

Although all the studies but one reported consistent results, we judged the overall certainty of evidence to be very low and downgraded by three levels for serious concerns regarding study limitations, indirectness and imprecision due to one study (Juarez 2013), at high risk of bias (as the principal investigator was responsible for all aspects of study, including implementation and follow-up for both the experimental and attention control groups, which were also highly imbalanced), the heterogeneous measures and reporting of results by different estimates that could not be pooled.

#### Cost

Only Grunfeld 2011 reported cost outcomes using quality-adjusted life years (QALY) to calculate the cost effectiveness of the use of a survivorship care plan after two years of follow-up among breast cancer survivors (408 participants). One QALY is equivalent to one year in perfect health and this study reported 1.42 QALY for the survivorship care plan arm and 1.41 QALY for the usual care only arm. We judged the certainty of evidence to be very low and downgraded by three levels for serious concerns regarding inconsistency, indirectness and imprecision since there was only one study.

### DISCUSSION

The aim of this systematic review was to summarise the available evidence regarding the effects of different follow-up strategies after curative primary cancer treatment in adult cancer survivors on the outcomes of overall survival, time to detection of recurrence, health-related quality of life, anxiety, depression and cost. Due to the wide range of follow-up strategies available, we categorised interventions into three groups based on whether the study investigated: 1) who leads the follow-up, 2) intensity of the followup strategy with regards to clinical examinations and diagnostic procedures, or 3) integration of other components to usual care that may be relevant for detection of recurrence, such as patient symptom education/monitoring or information through survivorship care plans. This focus reflects the 'who', 'what' and 'when' elements in Box 1. The 'where' is implied by who leads the follow-up (e.g. GP-led follow-up will take place in primary care), while the use of different formats/technologies to deliver care may vary across the same elements of follow-up and was not addressed in this review.

Although we were successful in pooling studies across cancer sites and were able to synthesise the evidence for different outcomes, we still could not provide conclusive evidence for the effect of certain intervention types on specific outcomes (e.g. effect of non-specialist-led follow-up on survival and detection of recurrence) due to the lack of available studies. However, identification of this knowledge gap across cancer sites is also an important part of this review. Below, we summarise our findings, discuss the strengths and limitations of this review and point to implications for future research and practice.

# **Summary of main results**

We identified 53 studies that evaluated three broad types of followup strategies.



# Non-specialist-led follow-up (i.e. GP-led, nurse-led, patient-initiated or shared care) versus specialist-led follow-up

We included 17 studies for this comparison. Four studies reported on overall survival, four studies reported on detection of recurrence, 13 studies reported on health-related quality of life, 14 studies reported on anxiety, 11 studies reported on depression and 8 studies reported cost.

It is uncertain how this strategy affects overall survival (HR 1.21, 95% CI 0.68 to 2.15; very low-certainty evidence) and time to detection of recurrence (data could not be pooled). This strategy may make little or no difference to health-related quality of life at 12 months (MD 1.06, 95% CI -1.83 to 3.95; low-certainty evidence), probably makes little or no difference to anxiety at 12 months (MD -0.03, 95% CI -0.73 to 0.67; moderate-certainty evidence) and has little or no effect on depression at 12 months (MD 0.03, 95% CI -0.35 to 0.42; high-certainty evidence). It is uncertain whether non-specialist-led follow-up is as cost-effective as specialist-led follow-up due to the substantial heterogeneity in how the included studies measured and reported this outcome.

# Less intensive versus more intensive follow-up (based on clinical visits, examinations or diagnostic procedures)

We included 24 studies for this comparison. Eighteen studies reported on overall survival, 22 studies reported on time to detection of recurrence, three studies reported on health-related quality of life, one study reported on anxiety, none of the studies reported on depression and six studies reported cost.

Less intensive follow-up may make little or no difference to overall survival (HR 1.05, 95% CI 0.96 to 1.14; low-certainty evidence) but probably increases time to detection of recurrence (HR 0.85, 95% CI 0.79 to 0.92; moderate-certainty evidence). Meta-regression analysis for both outcomes showed little or no difference in the intervention effect by cancer site, year of publication or quality score. However, the clinical relevance of a delay in detection of recurrence on patient outcomes is unclear as we did not analyse the two outcomes together. Sensitivity analysis gave a similar result for both outcomes. It is uncertain whether less intensive follow-up has an effect on health-related quality of life, anxiety and depression because the certainty of evidence is very low (and non-existent for the outcome of depression). All studies reported lower costs for the less intensive arm but there was substantial heterogeneity in how they measured and reported the outcome.

# Follow-up integrating additional patient symptom education or monitoring, or survivorship care plans versus usual care

We included 12 studies for this comparison. None of the studies reported on overall survival or detection of recurrence, all 12 studies reported on health-related quality of life, one study reported on anxiety, eight studies reported on depression and one study reported cost.

There is a lack of evidence for the effect of follow-up integrating additional patient symptom education or monitoring, or survivorship care plans on overall survival and time to detection of recurrence as none of the studies evaluated these outcomes. It is uncertain whether this strategy makes a difference to health-related quality of life, anxiety, depression and cost as the certainty of evidence is very low. There was substantial heterogeneity in how

the studies measured health-related quality of life and depression and only single studies reported anxiety and cost.

## Overall completeness and applicability of evidence

Thanks to the comprehensive search strategy, we have been able to identify, to the best of our ability, almost all the studies available that address the objectives of this review. We have also been able to pool the results of diverse interventions by constructing what we hope are three meaningful comparisons: 1) non-specialist-led versus specialist-led follow-up, 2) less intensive versus more intensive follow-up, and 3) follow-up integrating patient symptom education or monitoring, or survivorship care plans versus usual care only.

In this review, we include cancer sites that have not previously been represented. We also used more advanced statistical methods to include all possible data in the most appropriate way available (e.g. by estimating hazard ratios for time-to-event outcomes) and to investigate heterogeneity without splitting studies into subgroups and losing statistical power (e.g. using meta-regression). Furthermore, we analysed what might be considered the most important outcomes for patients, clinicians and health services, namely overall survival, detection of recurrence, quality of life, anxiety, depression and cost.

However, despite our efforts, the evidence presented in this review is limited by the fact that there is still a substantial lack of highquality research in many cancer sites and in many parts of the world. Although 12 cancer sites and 15 countries were represented in this review; the majority of the studies were in breast and colorectal cancer and almost all studies were carried out in highincome countries with universal healthcare systems, where there is a direct incentive to find the best model balancing cost and effect. Reasons for this may include the fact that trials are very expensive to carry out and relatively long follow-up periods are required for the outcomes of survival and recurrence, particularly in cancer sites with long survival and low recurrence rates. Thus, the evidence presented in this review may not be directly applicable in certain parts of the world and for certain cancer types. We also note that we only included studies carried out in participants with curativelytreated cancer. This means that our results cannot be generalised to the care of patients with late-stage or incurable cancer, which is characterised by further treatment and surveillance of progression rather than recurrence.

Finally, the broadness of our aims could only be achieved at the expense of specificity. Thus, we did not investigate more detailed aspects of an intervention, such as the effectiveness of tumour markers or specific types of imaging, nor did we investigate other outcomes, such as cancer-specific survival or the effects of early treatment for asymptomatic recurrences. We also did not investigate potential adverse effects of different follow-up strategies. However, we hope that the framework presented in the introduction and the results of this comprehensive review can provide the foundation for further work investigating more specific aspects of cancer follow-up.

# **Certainty of evidence**

As the evidence came from randomised trials, our quality assessments began at the highest level of certainty. However, after the GRADE assessment, the final certainty of evidence ranged from high to very low (Schünemann 2013). We have summarised



the GRADE certainty of evidence for each outcome in the three 'Summary of findings' tables: Summary of findings for the main comparison (non-specialist-led versus specialist-led follow-up), Summary of findings 2 (less intensive versus more intensive follow-up) and Summary of findings 3 (follow-up integrating additional patient symptom education or monitoring, or survivorship care plans versus usual care only). Details regarding the GRADE domains that we assessed and downgraded for each outcome are given in the footnotes of each 'Summary of findings' table and in the GRADE evidence profiles (Appendix 3).

It is worth noting that almost all the trials in this review were not blinded. In line with the judgement that the direction of bias is unclear (see Blinding (performance bias and detection bias)), we did not consider lack of blinding a serious enough concern to downgrade the certainty of evidence.

For non-specialist-led follow-up, the certainty of evidence for the effect on overall survival and detection of recurrence was very low, meaning that the synthesized results do not provide a reliable indication of the likely effect of this intervention. The certainty of evidence for the effect of this intervention was low on health-related quality of life, moderate for anxiety, high for depression and very low for cost. Thus, although we are relatively certain that this intervention does not worsen anxiety and depression for the patient, we are less certain about how it affects quality of life and cost.

For less intensive follow-up, the certainty of evidence for the effect on overall survival was low, mainly due to imprecision, as the confidence interval included a harm (potentially 3 extra deaths) that we judged to be important for patients and decision-makers. For time to detection of recurrence, the certainty of evidence was moderate, meaning that the estimated effect is likely to be close to the true effect. The certainty of evidence for the effect of this intervention on the rest of the outcomes was very low, and nonexistent for depression, highlighting our lack of knowledge on how this intervention impacts the patient's well-being.

For follow-up integrating patient education/monitoring and survivorship care plans, there was no evidence for the effect on overall survival and detection of recurrence, highlighting that we do not know how this newer type of follow-up strategy affects patient prognostic outcomes. The certainty of evidence for the effect of this intervention on the rest of the outcomes was very low, mainly due to the heterogeneous measures and time-points used in the different studies that could not be pooled in a meta-analysis.

#### Potential biases in the review process

We made several decisions and judgements in the review process that may have had an impact on our conclusions. Below, we identify and discuss the potential strengths and limitations of the review process using the domains identified in the tool to assess risk of bias in systematic reviews (ROBIS): study eligibility criteria, identification and selection of studies, data collection and study appraisal, synthesis and findings (Whiting 2016).

# Study eligibility criteria

Due to the broad objectives and research question of this review, all randomised trials comparing different types of follow-up with potential impact on detection of recurrence in patients who have undergone curatively-intended primary treatment were potentially

eligible. This led to the retrieval of a large number of studies comparing a wide range of interventions and measuring a wide range of outcomes. We adhered to our protocol by including only studies that reported on one of our pre-defined outcomes and we made the decision to exclude studies that did not integrate the intervention in clinical follow-up care even though they reported carrying out the intervention in participants undergoing follow-up after primary treatment. We based this decision on our judgement that outcomes in such studies were a measurement of purely the intervention (often a psychosocial or rehabilitation intervention), and not a measurement of a change in cancer follow-up per se. Furthermore, we included studies investigating a supportive care intervention only if there was a component that could be relevant for detection of recurrence, for example, symptom education and monitoring or survivorship care plans, in accordance with the focus of our review. We report the intervention components in detail for all the included studies in the Characteristics of included studies tables to help the reader navigate the specific comparisons.

#### **Identification and selection of studies**

We carried out the search with the support of our Cochrane editorial group, EPOC, and it included all the relevant databases. We did not place any restrictions on date, publication format or language. We also used additional searching methods, such as looking through references in commentaries, abstracts and articles, in order to retrieve as many potentially relevant studies as possible. In order to systematise the screening and selection process and minimise error in the inclusion of studies, we used the recommended software, Covidence, to ensure independent screening of each study by at least two review authors and we held regular discussion meetings with the review author group to resolve any uncertainties.

### Data collection and study appraisal

In order to systematise and minimise error, we used standardised data collection forms based on the EPOC template that we piloted and subsequently refined on the first five studies. For each study, one review author extracted all the pre-defined relevant data and another review author independently read all the publications from the same study and double-checked the form to ensure accuracy and that there were no missing data. Several review authors were involved in this process. At least two review authors independently carried out 'Risk of bias' assessments for each study and all the review authors took the online interactive learning modules developed by Cochrane Training (Page 2017; Sambunjak 2017), and read the relevant chapters in the Cochrane Handbook of Systematic Reviews of Interventions to minimise any error (Higgins 2011a; Higgins 2017). The review author group held regular discussion meetings regarding the studies and we resolved any issues through consensus. As we were interested in many outcomes, we also assessed the risk of bias in each domain by objective outcomes and patient-reported outcomes, so that we could draw clearer conclusions about any study limitations once we had synthesised the findings.

# **Synthesis and findings**

We made substantial efforts to include all the studies possible for the synthesis of each outcome by contacting study authors and using statistical methods to convert published data into estimates that we could pool. We addressed heterogeneity statistically, where possible, and have reported all findings either as metaanalyses or narrative summaries. We have reported the results



of each meta-analysis together with GRADE quality assessments and state MCIDs, where relevant, to help the reader draw the appropriate conclusions. At least two review authors carried out GRADE assessments for each outcome and the review authors took the online interactive learning modules developed by Cochrane Training (Page 2017; Sambunjak 2017), and read the relevant chapters in the *Cochrane Handbook for Systematic Reviews of Interventions* to minimise any error (Deeks 2017).

# Agreements and disagreements with other studies or reviews

To our knowledge, this is the first systematic review that comprehensively includes studies across follow-up interventions and across cancer sites, and pools their results for each outcome according to three groups of follow-up strategy. Our results extend the findings of the available Cochrane Reviews on cancer follow-up in breast, colorectal, cervical and ovarian cancer at the time of our search. However, although our findings regarding survival and quality of life are in line with the Cochrane Reviews on breast cancer and colorectal cancer follow-up, our finding of an effect on detection of recurrence was not found in the other two reviews.

In the Cochrane Review on follow-up strategies for breast cancer based on five included studies, Moschetti 2016 concluded that less intensive follow-up is just as effective as more intensive follow-up with regard to overall survival, time to detection of recurrence and quality of life. Their different result regarding time to detection of recurrence is probably due to the fact that they based their metaanalysis on only two studies (GIVIO 1994; Rosselli Del Turco 1994), and their result was borderline favouring more intensive followup (HR 0.84, 95% CI 0.71 to 1.00). In another systematic review of randomised trials investigating intensive breast cancer follow-up (Lafranconi 2017), which included six randomised trials (all of which were included in this review except Gulliford 1997), the authors concluded that more frequent diagnostic tests or visits did not have effects on overall mortality or recurrences. However, they summarised effects as dichotomous outcomes and presented them as risk ratios, thus differing from our time-to-event analyses.

In the Cochrane Review on follow-up strategies for colorectal cancer based on 15 included studies, Jeffery 2016 concluded that there was no overall survival or relapse-free survival benefit with more intensive follow-up. Their different result regarding detection of recurrence is likely due to the fact that they based their metaanalysis on different studies from ours. Five of our studies were from other cancer sites (GIVIO 1994; Picardi 2014; Rosselli Del Turco 1994; Rustin 2007; Westeel 2012) and we did not include seven of their studies (Augestad 2013; Mäkelä 1992; Ohlsson 1995; Pietra 1998; Schoemaker 1998; Secco 2002; Wang 2009). Augestad 2013 calculated recurrence from the time of suspicion of recurrence instead of from randomisation and although the authors of Jeffery 2016 kindly provided the methods they used when we contacted them, we could not obtain enough information from the latter five studies to estimate hazard ratios (see Effects of interventions, Comparison 2: less intensive versus more intensive follow-up, Time to detection of recurrence). We did not identify any new systematic reviews of randomised trials investigating colorectal cancer followup, other than the five that Jeffery 2016 identified, and we refer to the discussion in their review.

In the Cochrane Review on follow-up strategies for ovarian cancer, Clarke 2014 identified one study that was not included in

ours (Rustin 2010). This study investigated early versus delayed treatment of relapsed ovarian cancer and found that there was no overall survival benefit from immediate treatment based on raised CA125 levels compared to delayed treatment until a woman develops symptoms. As patients were only randomised after elevated serum levels were detected, we did not include this study, as we judged that the outcomes were a measure of the effect of an early versus later intervention in patients with recurrence, rather than of change in follow-up strategies among patients treated with curative intent. No studies were found in the Cochrane Review on follow-up strategies for cervical cancer (Lanceley 2013), while a Cochrane Review is underway investigating follow-up strategies for women with endometrial cancer (Aslam 2016).

We did not find any other systematic reviews focusing on randomised trials of follow-up strategies in specific cancer sites, but identified four other systematic reviews that included randomised trials across cancer sites. However, all four reviews did not carry out any meta-analyses and reported the results of the individual studies in narrative form. Lewis 2009a and Lewis 2009b reported on follow-up in primary care versus secondary care (11 randomised trials) and nurse-led versus conventional physician-led followup (four randomised trials) respectively. Conclusions in both publications are in line with our results except that they report "no statistically significant difference for recurrence rate." Dickinson 2014 carried out a systematic review on the use of technology to deliver cancer follow-up care (13 randomised trials) and concluded that the use of telephone follow-up or internet-based educational programmes were acceptable and feasible, based on the outcomes of patient satisfaction, quality of life and psychological distress. Barbieri 2018 carried out a systematic literature review on the costeffectiveness of follow-up strategies after cancer treatment based on 44 articles (including non-randomised trials). They concluded that intensive follow-up is likely to be cost-effective in colorectal cancer but not in breast cancer, and there was insufficient evidence to make conclusions for the other cancer sites.

# **AUTHORS' CONCLUSIONS**

### Implications for practice

In many high-income countries, conventional follow-up strategies, such as routine examination by a specialist, are being substituted with less intensive and allegedly more strategic approaches. In this context, it is important to evaluate whether these changes may lead to poorer prognosis and patient-reported outcomes. Our finding that less intensive strategies do not negatively affect overall survival may be considered reassuring, in light of this current trend.

Our finding that more intensive strategies detect recurrences earlier have less clear implications. As the two outcomes (recurrence and survival) were not analysed together, we cannot make direct conclusions about the effect of interventions on survival after detection of recurrence. In fact, the content and organisation of conventional follow-up strategies has long focused on the early detection of recurrences, based on the assumption that early detection of recurrence translates into longer survival through early treatment. As our review is the first to find an effect of less intensive strategies on recurrence, further knowledge is needed. We need more high-quality studies that use the appropriate approach to evaluate the effect of follow-up strategies on survival according to detection of recurrence status. Several mechanisms may be at play influencing survival after recurrence compared to overall survival. It



is possible that the biology of recurrences is different across cancer sites and that early detection and treatment of oligometastatic recurrence may lead to a survival benefit in some cancer sites but not in others.

Despite the lower certainty of the evidence, our results on quality-of-life and psychological distress indicate that we do not yet have sufficient knowledge on how to improve these aspects of cancer survivorship to an extent that shows a measurable effect. As we included only studies that focused on cancer follow-up and excluded studies that only focused on improving quality of life, it is possible that the components in the studies we included were too weak to make a difference. It is also possible that current measurement tools for quality of life, anxiety and depression are inadequate or not optimal for capturing the psychological changes that patients may experience.

In many countries, there is currently a discussion about whether the core focus of follow-up should be broadened from detection of recurrence to further include somatic and psychological late effects. It is thus important to know if it is possible to provide interventions that are able to significantly improve these patient-reported experiences. Concurrent with this discussion, it has also been suggested that patients should be more directly involved in their cancer follow-up, for example, through self-monitoring of symptoms and shared treatment decisions. This is a relatively new way of thinking about cancer follow-up care. A few of the studies included in this review tested some of these principles, for example, through patient education of symptom monitoring and patient-initiated contact with health professionals, but further theoretical and clinical development is needed to test ways of organising patient-centred cancer follow-up.

### Implications for research

Our evaluation of the evidence quality in this review indicates that there is still room for improvement in the quality of randomised trials in cancer follow-up. Although the blinding of participants often is not possible or ethical, other efforts could be made to minimise bias due to differential treatment or differential assessment of outcomes. Our review also highlights the need to use more optimal methods and statistical analyses where possible, as this has an important impact on the level of certainty of the evidence. Analysing time-to-event outcomes as continuous outcomes or dichotomous outcomes increases the risk of biased estimates, makes meta-analysis difficult and limits the conclusions that are able to be drawn, as a large amount of information from each study becomes lost. For example, reporting time to detection of recurrence as mean times to event may give inaccurate treatment effect estimates, as such analysis only takes into account the subset of participants who have had a recurrence and excludes those who remain cancer-free. Finally, reporting participant-years of follow-up when conducting survival analysis will help enhance the transparency of findings in clinical trials.

A possible direction for future research may be investigating the effect of early detection of recurrence on patient outcomes such as survival, when comparing more intensive and less intensive strategies. This may provide the knowledge needed for discussing how much clinical focus should be placed on detecting recurrence as early as possible. Several studies in this review have investigated detection of recurrence and overall survival, but not together.

Robust evidence will need to come from analyses using multistate models that take into account both the time to detection of recurrence and death for all participants. Although such studies will require a large amount of resources and long follow-up periods, they would provide the evidence needed to make the decisions that affect the lives of millions of cancer survivors. Such studies may also investigate any potential adverse effects of different follow-up strategies, an aspect that was outside the scope of this review.

Despite the relatively low level of evidence, our review indicates that we need more knowledge on how to improve and provide the necessary medical and psychosocial support that cancer survivors may need. Outcome measurement tools may also need to be developed specifically for the somatic and psychological symptoms in cancer survivors, as most of the outcome measures in the included studies were developed to capture symptoms during cancer treatment. Parallel to the discussion regarding higher levels of patient involvement in treatment, it has been suggested that involving patients in research may also be beneficial, especially when developing patient-centred interventions. This is a relatively new paradigm in research that is still being investigated.

In this review, we have identified many studies that contribute knowledge on a range of important outcomes in a large population of cancer survivors. We have also systematically identified knowledge gaps that remain to be filled. Future research may build and expand on the findings of this review, as well as improve on the limitations of our methods. This knowledge is needed to justify the enormous resources that are increasingly required to provide safe and effective follow-up for adult cancer survivors around the world.

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\* Indicates the major publication for the study

# CHARACTERISTICS OF STUDIES

**Characteristics of included studies** [ordered by study ID]

### **Augestad 2013**

Methods	Randomised trial			
	GP-led vs surgeon-led follow-up			
	Cancer site: colon cancer			
	Setting: multicenter trial at 3 local hospitals and 1 university hospital in Norway			
	Accrual: June 2007-December 2011			
	Duration of follow-up: 24 months ("1884 follow-up months")			
Participants	110 patients with recent surgery for colon cancer at Dukes' stage A, B or C			
	Age (mean/SD): 65.4 (8.1) years			
	Sex: 65 men, 45 women			
Interventions	Intervention group: GP-led follow-up, n = 55			
	<ul> <li>Comparison group: surgeon-led follow-up, n = 55</li> </ul>			
	"National follow-up guidelines (consultations and radiology with 6 months interval) were applied in both study arms and patients were followed up for up to 2 years"			
Outcomes	The primary outcome measure in this trial was the global health status on the EORTC QLQ C-30, Euro-Qol-5D, EQ VAS records the respondent's self-rated health status, cost-effectiveness, time to cancer diagnosis			
Funding	Northern Norway Health Authorities Research Fund			
Notes				

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The randomization service is web-based and managed by the Norwegian University of Science and Technology."
		Comment: as it is computer-based, we consider the risk of bias to be low.
Allocation concealment (selection bias)	Low risk	Quote: "The randomization service is web-based and managed by the Norwegian University of Science and Technology."
		Comment: as it was web-based, we consider the risk of bias to be low.
Blinding of participants and personnel (perfor- mance bias)	Unclear risk	Quote: "No information regarding trial progress and allocation was revealed to the participating GPs or surgeons. However, as GP organized follow-up represented a new practice, blinding was not possible in the intervention arm."



Augestad 2013 (Continued) Objective outcomes		Comment: given the nature of the study, it was not possible to blind participants or personnel.
Blinding of participants and personnel (perfor- mance bias) Patient-reported out- comes	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.
Blinding of outcome assessment (detection bias) Time-to-detection of recurrence	Unclear risk	Quote: "Resources used were registered prospectively based on reports by the patients and on hospital electronic medical record (EMR) review."  Comment: assessors were not blinded and some of the clinical outcomes were based on judgements, but the likely direction of bias cannot be predicted.
Blinding of outcome assessment (detection bias) Patient-reported outcomes	Unclear risk	Participants were self-assessors and were not blinded but the likely direction of bias cannot be predicted.
Incomplete outcome data (attrition bias) Objective outcomes	Low risk	Similar numbers and reasons for loss to follow-up
Incomplete outcome data (attrition bias) Patient-reported out- comes	Low risk	Similar response rates in both groups
Selective reporting (reporting bias)	Low risk	All outcomes described in the protocol/clinical trials entry were reported.
Other bias	Unclear risk	We detected no other bias.

# Beaver 2009

Methods	Randomised trial		
	Nurse-led telephone vs conventional specialist (hospital) follow-up		
Cancer site: breast cancer			
	Setting: outpatient clinics in 2 NHS hospital trusts in the north west of England (UK)		
	Accrual: 2003-2006		
Duration of follow-up: participants remained in the study for a mean of 24 months			
	(range 2-43 months)		
Participants	374 women treated for breast cancer who were at low to moderate risk of recurrence		
	Age (mean/range): 64.0 (36-93) years		
	Sex: 100% female		
Interventions	Intervention group: nurse-led telephone follow-up, n = 191		



### Beaver 2009 (Continued)

"Participants randomised to telephone follow-up received telephone appointments from breast care nurses at intervals consistent with hospital follow-up policy. Each individual telephone appointment was allocated 30 minutes; 20 minutes for conducting the consultation and 10 minutes to dictate the outcome of consultations. Standard protocols related to routine mammography were unaltered."

• Comparison group: hospital follow-up, n = 183

"At the district general hospital participants were reviewed every three months for two years, six monthly for two years, then annually for a further year. At the specialist breast unit they were reviewed annually for 10 years. Hospital consultations were generally unstructured but primarily consisted of a clinical examination, a check on whether hormone treatment was being taken as prescribed, and ordering mammograms if necessary."

Outcomes Psychological morbidity (STAI, GHQ-12), participants' needs for information, participants' satisfaction, clinical investigations ordered, time to detection of recurrent disease, and costs

The trial was funded by the Medical Research Council (UK) and a project grant from Rosemere Cancer Foundation (UK).

Notes

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Allocation sequences were computer generated with randomised permuted blocks."
Allocation concealment (selection bias)	Low risk	Quote: "Allocation sequences were concealed until interventions were assigned."
Blinding of participants and personnel (perfor- mance bias) Objective outcomes	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.
Blinding of participants and personnel (perfor- mance bias) Patient-reported out- comes	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.
Blinding of outcome assessment (detection bias) Time-to-detection of re-	Unclear risk	Quote: "A record of visit form recorded actions resulting from consultations and indicators of recurrence in the hospital arm. The recorded telephone appointments provided equivalent data."
currence		Comment: assessors were not blinded and some of the clinical outcomes were based on judgements, but the likely direction of bias cannot be predicted.
Blinding of outcome assessment (detection bias) Patient-reported outcomes	Unclear risk	Participants were self-assessors and were not blinded but the likely direction of bias cannot be predicted.
Incomplete outcome data (attrition bias) Objective outcomes	High risk	A study flow on page 4 shows more participants in the telephone follow-up did not receive the intervention or wanted to change group and were lost to follow-up. Furthermore, participants with no data were dropped with the assumption that data were missing at random, although it was reported that ITT analysis was performed.



Beaver 2009 (Continued)		
Incomplete outcome data (attrition bias) Patient-reported out- comes	High risk	A study flow on page 4 shows more participants in the telephone follow-up did not receive the intervention or wanted to change group and were lost to follow-up. Furthermore, participants with no data were dropped with the assumption that data were missing at random, although it was reported that ITT analysis was performed.
Selective reporting (reporting bias)	Unclear risk	No protocol available, however all outcomes mentioned in the aims were reported
Other bias	Unclear risk	Quote: "For practical reasons we could not administer outcome question- naires before randomisation. We sent initial questionnaires to patients imme- diately after randomisation, a minimum of three months before their next ap- pointment."
		Comment: baseline measures can be influenced due to lack of blinding but the direction of bias is difficult to predict.

# Beaver 2012

Methods	Randomised trial
	Nurse-led telephone vs conventional specialist (hospital) follow-up
	Cancer site: colorectal
	Setting: recruitment took place at a large hospital in the north-west of England (UK)
	Accrual: not reported
	Duration of follow-up: participants remained in the study from 8-15 months (mean 12 months)
Participants	65 patients who had completed treatment (surgery/radiotherapy/chemotherapy) with no evidence of recurrent disease
	Age (mean/SD): telephone group: 73.6 (7.6) years; hospital group: 72.4 (8.2) years
	Sex: 100% female
Interventions	Intervention group: telephone follow-up, n = 32
	"Participants randomized to telephone follow-up received telephone consultations from a colorectal nurse practitioner at the same prescribed intervals as participants in the hospital arm. Thirty minutes were allocated for telephone appointments (20 min consultation time, 10 min administration). Questions were asked relating to changes in condition, new or unresolved symptoms, information requirements about spread of disease, treatment and side-effects, genetic risk, sexual attractiveness, sexual function, self-care and family concerns. Standard protocols related to routine tests and investigations (e.g. carcinoembryonic antigen blood levels, CT scan, colonoscopy) were unaltered."
	• Comparison group: hospital follow-up, n = 33
	"Participants randomized to the hospital arm were routinely reviewed at 6-weeks posttreatment, then 6-monthly intervals for 2 years and annually for a further 3 years and discharged to the care of their general practitioner (GP) after 5 years. Clinicians focused on routine monitoring for detection of recurrent disease."
Outcomes	Primary outcomes included psychological morbidity (STAI, GHQ-12), meeting information needs and satisfaction with information and service. Secondary outcomes related to clinical investigations ordered, time to detection of recurrent disease and costs to participants.



# Beaver 2012 (Continued)

Funding This study was financially supported by a small project grant from Cancer Research UK.

Notes

Bias	Authors' judgement	Support for judgement	
Random sequence generation (selection bias)	Low risk	Quote: "Consenting individuals were randomized to either hospital or tele- phone follow-up by a computerized system."	
Allocation concealment (selection bias)	Low risk	Quote: "Allocation sequences were concealed until interventions were assigned."	
Blinding of participants and personnel (perfor- mance bias) Objective outcomes	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.	
Blinding of participants and personnel (perfor- mance bias) Patient-reported out- comes	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.	
Blinding of outcome assessment (detection bias) Time-to-detection of recurrence	Unclear risk	Assessors were not blinded and some of the clinical outcomes were based on judgements, but the likely direction of bias cannot be predicted.	
Blinding of outcome assessment (detection bias) Patient-reported outcomes	Unclear risk	Participants were self-assessors and were not blinded but the likely direction of bias cannot be predicted.	
Incomplete outcome data (attrition bias) Objective outcomes	Low risk	Similar numbers and similar reasons for attrition in both groups. All participants were followed up for recurrence.	
Incomplete outcome data (attrition bias) Patient-reported out- comes	High risk	Quote: "Not all participants provided complete data on the primary outcome measures. Only 12 (48%) hospital and 15 (60%) telephone participants provided complete data on the STAI at baseline and follow-up."	
comes		Comment: 25% of the participants in both groups were lost to follow-up. Although similar numbers were lost to follow-up the reasons were different.	
Selective reporting (reporting bias)	Unclear risk	No protocol available, however all outcomes mentioned in the aims were reported.	
Other bias	High risk	Quote: "The same nurse conducted some of the hospital appointments and all the telephone appointments. Although the nurse only used the structured telephone intervention with patients randomized to the telephone arm, contamination is possible and would need to be avoided in a main trial."	
		Comment: high risk of contamination	



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Methods	Randomised trial			
	Nurse-led telephone	vs conventional specialist (hospital) follow-up		
	Cancer site: endometri	ial cancer		
	Setting: 5 centres in th	e north-west of England (UK)		
	Accrual: January 2012-	January 2014		
		depended on whether women were on a 3–monthly, 6–monthly, or annual fol- d range from 3-12 months after baseline data collection		
Participants	259 stage I endometria	ll cancer patients		
	Age (median/IQR): 65 (	58-71) years		
	Sex: 100% female			
Interventions	Intervention group:	nurse-led telephone follow-up, n = 129		
	"In the TFU arm, a telephone intervention was delivered by gynaecology oncology nurse specialists at intervals consistent with hospital policy at the study locations. The intervention was designed to be delivered in 20 minutes. Questions in the intervention were focused on the physical, psychological, and social aspects of care."			
	• Comparison group: hospital follow-up, n = 130			
	"Patients allocated to HFU continued to receive hospital-based follow-up in accordance with hospital policy at the study locations. This consisted of appointments every 3 or 4 months for the first 2 years post-treatment followed by appointments at decreasing intervals (6–monthly and annually), up to a period of 3–5 years. Although there was no standard format to hospital-based consultations, they would usually include a clinical examination (bimanual examination and inspection of the vagina) and questions about any signs of recurrent disease."			
Outcomes	Primary outcomes were psychological morbidity (STAI–S) and participant satisfaction with the information provided. Secondary outcomes included participant satisfaction with service, QoL, time to detection of recurrence and costs			
Funding	NIHR under its Research for Patient Benefit (RfPB) programme (grant ref. no. PB-PG-0610-22123)			
Notes	This study did not provide the required data for inclusion in the meta-analyses.			
Risk of bias				
Bias	Authors' judgement	Support for judgement		
Random sequence generation (selection bias)	Low risk	Quote: "Patients were randomly assigned (1:1) to HFU or TFU using a computer-based system."		
Allocation concealment (selection bias)	Low risk	Quote: "Patients were randomly assigned (1:1) to HFU or TFU using a computer-based system."		
		Comment: as it was computer-based, we consider the risk of bias to be low.		
Blinding of participants and personnel (perfor- mance bias) Objective outcomes	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.		



Beaver 2017 (Continued)		
Blinding of participants and personnel (perfor- mance bias) Patient-reported out- comes	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.
Blinding of outcome assessment (detection bias) Time-to-detection of recurrence	Unclear risk	Assessors were not blinded and some of the clinical outcomes were based on judgements, but the likely direction of bias cannot be predicted.
Blinding of outcome assessment (detection bias) Patient-reported outcomes	Unclear risk	Participants were self-assessors and were not blinded but the likely direction of bias cannot be predicted.
Incomplete outcome data (attrition bias) Objective outcomes	Low risk	Similar numbers and reasons for loss to follow-up
Incomplete outcome data (attrition bias) Patient-reported out- comes	Low risk	Similar response rates in both groups
Selective reporting (reporting bias)	Unclear risk	No protocol available, however all outcomes mentioned in the aims were reported.
Other bias	Unclear risk	Quote: "It was not possible to recruit all participants immediately after their first post-treatment outpatient appointment. Although 51% of women were <1 year post surgery, many would have experienced a number of hospital outpatient appointments, and this may have biased the outcomes. Given that women would have experienced at least one hospital appointment prior to recruitment it is not possible to state when the introduction of TFU would be most beneficial or if the findings are generalizable to the first follow-up appointment."
		Comment: possible carry-over effect may attenuate the effect of the intervention.

# Brown 2002

Methods	Randomised trial		
	Patient-initiated vs conventional specialist (standard clinic) follow-up		
	Cancer site: breast cancer		
Setting: 4 clinics at the Royal South Hants Hospital in Southampton and a clinic at Lyming UK			
	Accrual: not reported		
	Duration of follow-up: 12 months		
Participants	61 women treated for Stage I breast cancer		
	Age (mean): 65.34 years		



Brown 2002	(Continued)	)
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Sex: 100% female

### Interventions

- Intervention group: participant-initiated follow-up, n = 30
- "Patients received written information on the signs and symptoms of recurrence (see Table 1). They did not attend the routine clinic appointments and were advised to contact the Breast Care Nurse (BCN) by telephone if they experienced a problem. They still received their yearly mammogram."
- Comparison group: standard clinic follow-up, n = 31

"Standard clinic follow up where the participants attended the clinic as usual. Here, they were examined by a doctor and had the opportunity to ask questions."

### Outcomes

QoL (EORTC) QLQ-C30 and QLQBR23), psychological morbidity (HADS), satisfaction with the type of outpatient follow up received

**Funding** 

Not reported

Notes

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "A random number list generated by the Medical Statistics Department at Southamp- ton General Hospital was used."
Allocation concealment (selection bias)	Unclear risk	Concealment not reported
Blinding of participants and personnel (perfor- mance bias) Patient-reported out- comes	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.
Blinding of outcome assessment (detection bias) Patient-reported outcomes	Unclear risk	Participants were self-assessors and were not blinded, but the likely direction of bias cannot be predicted.
Incomplete outcome data (attrition bias) Patient-reported outcomes	Low risk	Similar numbers and reasons for loss to follow-up in both groups
Selective reporting (reporting bias)	Unclear risk	No protocol available, however all outcomes mentioned in the aims were reported
Other bias	Unclear risk	Quote: "As recruitment was difficult the resulting sample size was small and although power calculations were not performed, the study was almost certainly underpowered. Presentation bias may have influenced responses to the interview questions regarding satisfaction."
		Comment: the direction of bias is difficult to predict.



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Methods	Randomised trial  More intensive (physical examination plus ultrasonography) vs physical examination only  Cancer site: oral cancer			
	Setting: Tata Memorial	Hospital, Mumbai, India		
	Accrual: January 2004-	June 2014		
	Duration of follow-up:	median of 39 months		
Participants	496 patients with later of primary with/withou	alised T1 or T2 squamous carcinoma of oral cavity after initial surgery (excision at neck dissection)		
	Age (mean/range): 48 (	20–75) years		
	Sex: 24.6% women, 75.	.4% men		
Interventions	Intervention group:	physical examination plus ultrasonography, n = 252		
	followed with first visit	d to routine clinical examination in early detection of metastasis. Patients were at 4 weeks, for the first 6 months every 4-6 weeks, from 6-12 months every 6-8 s to 2 years every 8-12 weeks and thereafter 3 monthly."		
	Comparison group:	physical examination only, n = 244		
	"Physical examination is usual care. Patients were followed with first visit at 4 weeks, for the first 6 months every 4-6 weeks, from 6-12 months every 6-8 weeks, from 12 months to 2 years every 8-12 weeks and thereafter 3 monthly."			
Outcomes	Overall survival			
Funding	Tata Memorial Hospital			
Notes	Abstract only, full report not yet published. This randomised trial on follow-up was carried out within a prior trial comparing elective and therapeutic neck dissection (see reference list).			
Risk of bias				
Bias	Authors' judgement	Support for judgement		
Random sequence generation (selection bias)	Low risk	Participants were randomised with the use of a prepared computerised block design.		
Allocation concealment (selection bias)	Low risk	It is not clear whether or not the allocation was concealed. We assume that the computerised design ensured allocation concealment.		
Blinding of participants and personnel (perfor- mance bias) Objective outcomes	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.		
Blinding of outcome assessment (detection bias) Overall survival	Low risk	The outcome of survival is not expected to be biased.		
Incomplete outcome data (attrition bias) Objective outcomes	Low risk	Similar numbers and reasons for loss to follow-up in both groups were reported in the publication reporting on the randomised trial comparing elective surgery or therapeutic surgery. As the randomisation to follow-up was carried		



D'Cruz 2016 (Continued)		out in the same population, we assume that the numbers and reasons remain the same.
Selective reporting (reporting bias)	Low risk	All outcomes described in the protocol were reported.
Other bias	Unclear risk	We detected no other bias.

# Damude 2016

Methods	Randomised trial
	Less frequent vs conventional follow-up schedule
	Cancer site: cutaneous melanoma
	Setting: 6 hospitals in the Netherlands
	Accrual: all patients treated between February 2006 and November 2013
	Duration of follow-up: 12 months
Participants	180 patients diagnosed with AJCC stage IB-II cutaneous melanoma, treated with curative intent
	Age (median): 57.4 years
	Sex: 51.7% women, 48.3% men
Interventions	<ul> <li>Intervention group: experimental follow-up schedule, n = 87</li> </ul>
	"The experimental schedule was defined with an overall reduction of 27 $\%$ of the number of conventional schedule visits during the first 5 years after diagnosis"
	<ul> <li>Comparison group: conventional follow-up schedule, n = 93</li> </ul>
	"The conventional follow-up schedule was according to Dutch Melanoma guideline recommendations"
Outcomes	Anxiety (STAI-S; 3-item CWS, assessing concerns about developing cancer (again) and their impact on daily functioning; 15-item IES, assessing the extent to which people are bothered by memories of a major life-event in terms of intrusion and avoidance); HRQoL (MCS score of the RAND-36); time to detection of recurrence and costs
Funding	Not reported
Notes	

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Randomization was performed in random permuted blocks of four patients, generated by a validated system (Intrialgrator) with the use of a pseudo-random number generator and a supplied seed number. Randomization and data management were performed by the Netherlands Comprehensive Cancer Organization (IKNL)."
Allocation concealment (selection bias)	Low risk	Quote: "Randomization and data management were performed by the Netherlands Comprehensive Cancer Organization (IKNL)."



Blinding of participants and personnel (performance bias) Objective outcomes    Unclear risk and personnel (performance bias) Objective outcomes    Unclear risk and personnel (performance bias)   Patient-reported outcomes	Damude 2016 (Continued)		
and personnel (performance bias) Patient-reported outcomes  Blinding of outcome assessment (detection bias) Time-to-detection of recurrence  Unclear risk  Blinding of outcome assessment (detection bias) Time-to-detection of recurrence  Unclear risk  Unclear risk  Unclear risk  Dime-to-detection of recurrence  Unclear risk  Blinding of outcome assessment (detection bias) Time-to-detection of recurrence  Unclear risk  Dime-to-detection of recurrence  Unclear risk  Unclear risk  Participants were not blinded and as some of the clinical outcomes were based on judgements, the likely direction of bias cannot be predicted.  Participants were self-assessors and were not blinded but the likely direction of bias cannot be predicted.  Participants were self-assessors and were not blinded but the likely direction of bias cannot be predicted.  Unclear risk  We are unable to judge whether reasons for loss to follow-up are similar in the 2 groups as study flow in figure 1 does not follow the CONSORT structure. However, levels of attrition appear low.  Incomplete outcome data (attrition bias) Patient-reported outcome data (attrition bias) Patient-repo	and personnel (perfor- mance bias)	Unclear risk	
ing follow-up, registered melanoma-related variables, and the actual frequency of melanoma-related follow-up visits in the hospital. Laboratory testing and diagnostic imaging was only performed in patients suspicious for recurrent disease, as appropriate."  Comment: assessors were not blinded and as some of the clinical outcomes were based on judgements, the likely direction of bias cannot be predicted.  Blinding of outcome assessment (detection bias) Patient-reported outcomes  Incomplete outcome data (attrition bias) Objective outcomes  Low risk  We are unable to judge whether reasons for loss to follow-up are similar in the 2 groups as study flow in figure 1 does not follow the CONSORT structure. However, levels of attrition appear low.  Low risk  Quote: "Of the participants, 83 % completed all questionnaires at T1 and T2 (CSG: n = 76, ESG: n = 73). PROMs were analyzed for these 149 participants."  Comment: similar response rates in both groups  Selective reporting (reported)  No protocol available, however all outcomes mentioned in the aims were reported	and personnel (perfor- mance bias) Patient-reported out-	Unclear risk	
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(attrition bias) Patient-reported outcomes  Comment: similar response rates in both groups  Selective reporting (reporting bias)  Comment: where analyzed for these 149 participants."  Comment: similar response rates in both groups  No protocol available, however all outcomes mentioned in the aims were reported	(attrition bias)	Low risk	the 2 groups as study flow in figure 1 does not follow the CONSORT structure.
porting bias) ported	(attrition bias) Patient-reported out-	Low risk	(CSG: n = 76, ESG: n = 73). PROMs were analyzed for these 149 participants."
Other bias Unclear risk We detected no other bias.		Unclear risk	•
	Other bias	Unclear risk	We detected no other bias.

# **Davis 2013**

Methods	Randomised trial		
	Addition of technology-assisted symptom monitoring vs usual care follow-up		
	Cancer site: prostate cancer		
	Setting: participants were recruited from urologists and radiation oncologists at 2 affiliated hospitals in the Washington, DC metropolitan area: Georgetown University Medical Center (GUMC) and Washington Hospital Center (WHC).		
	Accrual: not reported		
	Duration of follow-up: 7 months		
Participants	94 early-stage prostate cancer survivors		
	Age (mean/SD): 62 (7.5) years		



### Davis 2013 (Continued)

Sex: 100% men

### Interventions

• Intervention group: symptom monitoring plus feedback (SM+F), n = 49

"Participants received written and verbal (by telephone) instructions on how to use the technology-assisted monitoring system. SMF participants were instructed to call the automated system 3 business days prior to their next 2 follow-up visits with their physician. For the monitoring intervention, the men completed the Prostate Cancer Subscale (PCS) of the Functional Assessment of Cancer Therapy-Prostate (FACT-P), a 12-item subscale that measures problems specific to prostate cancer. Participants completed the PCS via telephone by responding to questions using their keypad. The responses were stored in a database from which individualized reports were generated. The resident assistant delivered the reports to the physician approximately 24 hours prior to the scheduled follow-up visit."

• Comparison group: usual care, n = 93

"UC [usual care] participants saw their physicians as scheduled but did not use the monitoring system before each follow-up visit and no feedback was provided to physicians"

### Outcomes

General HRQoL (SF-12)

Cancer-specific HRQoL (FACT-G)

Prostate cancer-specific HRQoL (UCLA-PCI)

Doctor/patient communication (PCAS)

Post-visit ratings

Patient/physician study evaluation

### **Funding**

Grant from the National Cancer Institute R03 - CA119765-01A1a

Notes

This study did not provide the required data for inclusion in the meta-analyses.

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Randomization was conducted using the telephone-based system stored on a server at GUMC."
Allocation concealment (selection bias)	Low risk	Since it was telephone-based, we assume that the sequence was concealed.
Blinding of participants and personnel (perfor- mance bias) Patient-reported out- comes	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.
Blinding of outcome assessment (detection bias) Patient-reported outcomes	Unclear risk	Participants were self-assessors and were not blinded but the likely direction of bias cannot be predicted.
Incomplete outcome data (attrition bias) Patient-reported out- comes	Low risk	Approximately similar response rates and loss to follow-up reasons in the 2 groups.



Davis 2013 (Continued)		
Selective reporting (reporting bias)	Unclear risk	No protocol available, however all outcomes mentioned in the aims were reported.
Other bias	Unclear risk	We detected no other bias.

# **Emery 2016**

Methods	Randomised trial
	Shared care vs usual conventional specialist (hospital) follow-up
	Cancer site: prostate cancer
	Setting: men were recruited from 2 rural and 4 urban treatment centres in Victoria and Western Australia
	Accrual: November 2011 and July 2013
	Duration of follow-up: 12 months
Participants	88 men who had completed treatment for low- to moderate-risk prostate cancer
	Age (mean/SD): shared care group: 67.4 (7.0) years; hospital group: 65.8 (8.2) years
	Sex: 100% men
Interventions	Intervention group: shared care, n = 45
	"Two of the routine hospital visits during the first 12 months of follow-up were replaced by GP visits (at 6 and 9 months) and one additional GP visit shortly after completion of treatment. Five components were designed to facilitate shared care: (i) structured systematic communication, using a survivorship care plan (SCP; specific versions for the GP and the participant); (ii) GP clinical management guidelines and local resources; (iii) a register and recall system to prompt the participant and his GP about follow-up appointments; (iv) screening for distress and unmet needs; and (v) patient information resources about prostate cancer and treatment side-effects."
	<ul> <li>Comparison group: usual hospital care, n = 43</li> </ul>
	"Clinical care according to current hospital practice with visits every 3 months to the treating urologist or radiation oncologist team, consistent with international guidelines. These visits included a PSA test, review of any symptoms and clinical examination, where indicated."
Outcomes	Psychological distress (14-item HADS). Unmet needs (CaSUN). Prostate cancer-specific QoL ((EPIC). Participant satisfaction with care (18-item SF-PSQ-18)
Funding	This trial is supported by the National Health and Medical Research Council (grant ID 1003414). Associate Professor Schofield and Associate Professor Pirotta are supported by National Health and Medical Research Council Career Development Fellowships.
Notes	
Risk of bias	
Bias	Authors' judgement Support for judgement

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Randomization was performed using a centralized independent telerandomization system at the National Health and Medical Research Council (NHMRC)."



Allocation concealment (selection bias)  Low risk  Quote: "Randomization was performed using a centralized independent telerandomization system at the National Health and Medical Research Council (NHMRC)."  Blinding of participants and personnel (performance bias) Objective outcomes  Blinding of participants and personnel (performance bias) Patient-reported outcome assessment (detection bias) Time-to-detection of recurrence  Blinding of outcome assessment (detection of recurrence  Blinding of outcome assessment (detection bias) Patient-reported outcome ata (attrition bias) Patient-reported outcome data (attrition bias) Dipicative outcomes  Low risk  Similar numbers and reasons for loss to follow-up in the 2 groups  Incomplete outcome data (attrition bias) Patient-reported outcome  Low risk  Similar response rates in the 2 groups  Similar response rates in the 2 groups  Similar response rates in the protocol.  Divident risk  We detected no other bias.	Emery 2016 (Continued)		
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and personnel (performance bias) Patient-reported outcomes  Blinding of outcome assessment (detection bias) Time-to-detection of recurrence  Blinding of outcome assessment (detection bias) Time-to-detection of recurrence  Blinding of outcome assessment (detection bias) Patient-reported outcomes  Incomplete outcome data (attrition bias) Objective outcomes  Low risk  Similar numbers and reasons for loss to follow-up in the 2 groups  (attrition bias) Patient-reported outcomes  Similar response rates in the 2 groups  Similar response rates in the 2 groups  The study reports results on all outcomes described in the protocol.	and personnel (perfor- mance bias)	Unclear risk	
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(attrition bias) Patient-reported outcomes  Selective reporting (reporting bias)  The study reports results on all outcomes described in the protocol.	(attrition bias)	Low risk	Similar numbers and reasons for loss to follow-up in the 2 groups
porting bias)	(attrition bias) Patient-reported out-	Low risk	Similar response rates in the 2 groups
Other bias Unclear risk We detected no other bias.		Low risk	The study reports results on all outcomes described in the protocol.
	Other bias	Unclear risk	We detected no other bias.

# Gambazzi 2018

Methods	Randomised trial		
	More intensive vs less intensive diagnostic procedures (PET-CT vs CE-CT)		
	Cancer site: NSCLC		
	Setting: Cantonal Hospital Aarau, Switzerland		
	Accrual: October 2011-August 2014		
	Duration of follow-up: 2 years		
Participants	98 participants, age ≥ 18 years, had an 18F-FDG–PET–positive tumor, had a tumor stage of I-III (or IV, if patients presented with solitary, completely resected brain metastases), and had completed a curative-intent treatment for NSCLC		
	Age (mean/range):		



### Gambazzi 2018 (Continued)

PET-CT group: 67 (61-74) years

CE-CT group: 61 (56-70) years

Sex:

PET-CT group: 33 men 17 women

CE-CT group: 34 men 12 women

### Interventions

- Intervention group: PET-CT group, n = 50
- Comparison group: CE-CT group, n = 48

During the 2-year follow-up period, a clinical examination and the respective imaging procedure were performed at 6-month intervals. If there was radiologic suspicion of cancer recurrence, the participant completed the study and underwent a diagnostic workup, which consisted of at least 1 of the following procedures: nonscheduled PET-CT or CE-CT scan, nonscheduled brain CT, bronchoscopy, or therapeutic-intent surgical intervention. Cancer recurrence was to be confirmed histologically unless there was clear evidence of metastatic disease.

Outcomes

The sensitivity, specificity, and positive predictive value for detecting cancer recurrence

**Funding** 

Research Funding from the Research Council of the Cantonal Hospital Aarau, Switzerland (Grant

14100.000.007).

### Notes

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The randomization process was computerized and generated on Excel software (Microsoft, Redmond, WA), without blocking."
Allocation concealment (selection bias)	Low risk	The randomisation process was computerised so we assume that allocation was concealed although not specifically reported
Blinding of participants and personnel (perfor- mance bias) Objective outcomes	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.
Blinding of outcome assessment (detection bias) Time-to-detection of recurrence	Unclear risk	Assessors were not blinded and as some of the clinical outcomes were based on judgements, the likely direction of bias cannot be predicted.
Incomplete outcome data (attrition bias) Objective outcomes	Low risk	All randomised participants were included in the analyses except 2 who declined to participate in the control group.
Selective reporting (reporting bias)	Unclear risk	No protocol available however they do report on the outcomes mentioned in the aims
Other bias	Unclear risk	We detected no other bias.



### **GILDA 2016**

# Methods Randomised trial More intensive diagnostic procedures vs minimal follow-up Cancer site: colorectal cancer Setting: 41 centres in 3 countries (Italy, 1199 participants; Spain, 41 participants; USA, 2 participants) Accrual: April 1998-September 2006 Duration of follow-up: 5 years or until relapse/diagnosis of new cancer Participants 1242 men who had adenocarcinoma of the colon or rectum with Dukes Astler-Coller modification stage B2-C treated with curative intent Age (median): intensive programme: 64.3 years; minimal programme 63.5 years Sex: 61% men, 39% women

### Interventions

• Intervention group: intensive programme, n = 622

All the patients were scheduled to have routine surveillance (medical history and physical examination).

**For colon cancer the intensive program included**: Office visit, CBC, CEA+CA19-9 at 4, 8, 12, 16, 20, 24, 30, 36, 42, 48 and 60 months after randomization

Colonoscopy Chest X-ray at 12, 24, 36, 48 and 60 months after randomization

Liver ultrasonography\* at 4, 8, 12, 16, 24, 36, 48 and 60 months

\*abdominal-pelvis CT, as an alternative to ultrasonography, was a 2° level exam only (doubtful results of physical examination or ultrasonography; increasing levels of CEA; predictable poor sensitivity of ultrasonography due to obesity or other anatomic-clinical conditions).

**For rectal cancer the intensive program included:** Office visit+digital rectal examination, CBC, CEA +CA 19-9 at 4, 8, 12, 16, 20, 24, 30, 36, 42, 48 and 60 months after randomization.

Proctoscopy at 4 and 8 months after randomization.

Colonoscopy, chest X-Ray at 12, 24, 36, 48 and 60 months after randomization.

Liver ultrasonography at 4, 8, 12, 16, 24, 36, 48 and 60 months after randomization.

Abdominal-pelvic C.T. at 4, 12, 24, 48 months after randomization.

• Comparison group: minimal programme, n = 620

All the patients were scheduled to have routine surveillance (medical history and physical examination).

### For colon Cancer the minimal program included:

Office visit, CEA at 4, 8, 12, 16, 20, 24, 30, 36, 42, 48 and 60 months after randomization.

Colonoscopy and chest X-ray at 12, 24, 36, 48 and 60 months after randomization.

Liver Ultrasonography at 4, and 16 months after randomization.

**For rectal cancer the minimal program included**: Office visit+digital rectal examination, CEA at 4, 8, 12, 16, 20, 24, 30, 36, 42, 48 and 60 months after randomization,

Proctoscopy 4 months after randomization,



GILDA 2016 (Continued)	Colonoscopy at 12 and 48 months after randomization, Chest X-ray 12 months after randomization and, liver ultrasonography at 8 and 16 months after randomization
Outcomes	Main end points were overall survival (OS) and HRQoL as reported by the participants. Secondary end points were the lead time due to the intensive programme, the incidence of recurrence, metachronous carcinoma, and other conditions liable to benefit from curative-intent resection, the sensitivity (the capability of diagnosing asymptomatic metastases), physician compliance with the surveillance programmes and QoL.
Funding	Istituto di Ricovero e Cura a Carattere Scientifico (IRCCS)
	Mario Negri Institute, Milan, Italy
Notes	

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Randomization was performed centrally via telephone at the Mario Negri Institute, Milan, Italy"
Allocation concealment (selection bias)	Low risk	Quote: "Randomization was performed centrally via telephone at the Mario Negri Institute, Milan, Italy"
Blinding of participants and personnel (perfor- mance bias) Objective outcomes	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.
Blinding of participants and personnel (perfor- mance bias) Patient-reported out- comes	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.
Blinding of outcome as- sessment (detection bias) Overall survival	Low risk	The outcome of survival is not likely to be biased.
Blinding of outcome as- sessment (detection bias) Time-to-detection of re- currence	Unclear risk	Assessors were not blinded and some of the clinical outcomes were based on judgements, but the likely direction of bias cannot be predicted.
Blinding of outcome as- sessment (detection bias) Patient-reported out- comes	Unclear risk	Participants were self-assessors and were not blinded, but the likely direction of bias cannot be predicted.
Incomplete outcome data (attrition bias) Objective outcomes	Low risk	Similar reasons and number of withdrawals and exclusions in each group
Incomplete outcome data (attrition bias) Patient-reported out- comes	Low risk	The overall response rate to the questionnaires were 80%.



GII	DA	2016	(Continued)

Selective reporting (re-	
porting bias)	

Low risk

The study reports results on all outcomes described in the protocol, although data on HRQoL is only reported using bar charts with no estimates in the text: "There were no clinically significant differences among the three main QoL scales for patients assigned to the minimal or intensive programs (Figure 4)."

Other bias Unclear risk We detected no other bias.

## **GIVIO 1994**

Methods	Randomised trial	
	More intensive diagnostic tests vs minimal follow-up	
	Cancer site: breast cancer	
	Setting: multicenter study involving 26 general hospitals in Italy	
	Accrual: September 1986-July 1988	
	Duration of follow-up: median follow-up of 71 months (range 59-81 months)	
Participants	1320 women < 70 years with stage I, II, and III unilateral primary breast cancer	
	Age: not reported	
Interventions	Intervention group: intensive programme, n = 655	
	"Routine medical visits (every 3 months for 3 years and every 6 months until year 5) plus a series of diagnostic tests targeted at detecting metastatic cancer (chest roentgenography, bone scan, liver echography and blood test). Yearly mammography."	
	• Comparison group: control "minimal" group, n = 665	
	"Routine medical visits (every 3 months for 3 years and every 6 months until year 5) and yearly mammography."	
Outcomes	5-year overall survival and HRQoL (Functional Living Index-Cancer Scale, Sickness Impact Profile, POMS, and the Cancer Inventory of Problem Situation)	
Funding	Italian National Research Council Special Projects Oncology Grant 88.00905.44, ACRO grant 92.02385.PF39, the National Cancer Institute grant CA45638-01 and a contribution by Zeneca Pharmaceuticals, Milan, Italy	

### Risk of bias

Notes

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Randomization was performed centrally via telephone using computer-generated lists."
Allocation concealment (selection bias)	Low risk	Quote: "Randomization was performed centrally via telephone using computer-generated lists."
Blinding of participants and personnel (perfor- mance bias)	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.



<b>GIVIO 1994</b> (Continued) Objective outcomes		
Blinding of participants and personnel (perfor- mance bias) Patient-reported out- comes	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.
Blinding of outcome assessment (detection bias) Overall survival	Low risk	The outcome of survival is not likely to be biased.
Blinding of outcome assessment (detection bias) Time-to-detection of recurrence	Unclear risk	Assessors were not blinded and some of the clinical outcomes were based on judgements, but the likely direction of bias cannot be predicted.
Blinding of outcome assessment (detection bias) Patient-reported outcomes	Unclear risk	Participants were self-assessors and were not blinded, but the likely direction of bias cannot be predicted.
Incomplete outcome data (attrition bias) Objective outcomes	Unclear risk	As participants lost to follow-up were not reported by group, it is difficult to assess risk of bias.
Incomplete outcome data (attrition bias) Patient-reported outcomes	Unclear risk	As participants lost to follow-up were not reported by group, it is difficult to assess risk of bias.
Selective reporting (reporting bias)	Unclear risk	No protocol available, however all outcomes mentioned in the aims were reported.
Other bias	Unclear risk	We detected no other bias

## **Grunfeld 1996**

Methods	Randomised trial  GP-led vs conventional specialist (hospital) follow-up			
	Cancer site: breast cancer			
	Setting: 2 district general hospitals in England, UK			
	Accrual: not reported			
	Duration of follow-up: 18 months			
Participants	296 women with stage I, II, or III breast cancer; no distant metastases			
	Age (mean/SD): GP group: 59.1 (10.3) years; hospital group 62.4 (12.0) years			
Interventions	Intervention group: GP-led follow-up, n = 148			
	• Comparison group: hospital follow-up, n = 148			



#### Grunfeld 1996 (Continued)

"The recommended frequency of routine visits in general practice was the same as for women remaining in hospital follow up and depended on the time since breast cancer had been diagnosed.

In one hospital the recommended follow up schedule after diagnosis was every three months for year 1, every six months for years 2-5, and every year thereafter; in the other it was every three, four, and six months for years 1, 2, and 3 respectively and every year thereafter. Mammography was recommended routinely every 12-36 months in one hospital (depending on initial treatment and age). For patients in the general practice group from this hospital all routine and diagnostic mammograms were initiated by the general practitioner. In the other hospital mammography was recommended routinely one year after completion of primary treatment and then every two years. Routine mammograms were organised through the breast cancer screening office and patients were recalled at the appropriate interval, but diagnostic mammography was initiated by the general practitioner for patients in the general practice group. All other investigations were recommended only if clinically indicated."

Outcomes Time between first presentation of symptoms to confirmation of recurrence; QoL (specific dimensions of SF-36, EORTC symptom scale, HADS), costs

The research was funded by the Department of Health for England and Wales with a generous contribution from Ballakermean School on the Isle of Man and support from the general practice research group of the Imperial Cancer Research Fund.

This study did not provide the required data for inclusion in the meta-analyses.

#### Risk of bias

**Funding** 

Notes

Bias	Authors' judgement	Support for judgement
Random sequence genera-	Low risk	Quote: "Random allocation was in blocks of eight."
tion (selection bias)		Comment: although sequence generation was not reported we consider the risk of bias to be low.
Allocation concealment (selection bias)	Low risk	Quote: "Follow up groups were assigned by a telephone call to the trial coordination centre in Oxford."
Blinding of participants and personnel (perfor- mance bias) Objective outcomes	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.
Blinding of participants and personnel (perfor- mance bias) Patient-reported out- comes	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.
Blinding of outcome assessment (detection bias) Time-to-detection of recurrence	Unclear risk	Assessors were not blinded and some of the clinical outcomes were based on judgements, but the likely direction of bias cannot be predicted.
Blinding of outcome assessment (detection bias) Patient-reported outcomes	Unclear risk	Participants were self-assessors and were not blinded, but the likely direction of bias cannot be predicted.
Incomplete outcome data (attrition bias) Objective outcomes	Low risk	No study flow but similar numbers and reasons were reported for loss to fol- low-up



Grunfeld 1996 (Continued)		
Incomplete outcome data (attrition bias) Patient-reported out- comes	Low risk	Quote: "The response rates in the in GP and hospital group respectively were: 99.3% (147/148) and 95.3% (141/148) at baseline, 97.2% (140/144) and 88.7% (126/142) at mid-trial, and 97.2% (137/141) and 88.1% (119/135) at the end of the trial."
Selective reporting (reporting bias)	Unclear risk	No protocol available, however all outcomes mentioned in the aims were reported.
Other bias	Unclear risk	Quote: "Baseline imbalances were reported with regard to age and disease stage I. As there was no common clinical examination at the end of the trial, it could be argued that there were unrecognised cases of recurrence in the general practice group which would have been elicited by examination at the hospital."  Comment: risk is unclear.

### **Grunfeld 2006**

Methods	Randomised trial  GP-led vs conventional specialist (hospital) follow-up			
	Cancer site: breast cancer			
	Setting: 6 of 9 regional cancer centres in Ontario, Canada			
	Accrual: January 1997-June 2001			
	Duration of follow-up: participants were observed until June 2003			
Participants	968 women with early stage breast cancer, who were disease-free			
	Age (mean): 61 years			
Interventions	Intervention group: family physician follow-up, n = 483			
	"Family physicians were provided with a guideline on follow-up that recommended the following: physical examination and medical history every 3 to 6 months for 3 years, every 6 months for 2 years, and then yearly indefinitely; mammograms yearly; diagnostic tests to investigate signs or symptoms suggestive of recurrent or new primary cancer, but such tests were not to be performed routinely. For women taking tamoxifen, the guideline recommended that a history of vaginal bleeding be taken at each visit and a pelvic examination be performed annually. Family physicians were instructed to refer patients back to the cancer center if a recurrence or new primary breast cancer developed."			
	<ul> <li>Comparison group: cancer centre usual practice, n = 485</li> </ul>			
	Same as above.			
Outcomes	Primary outcome: a recurrence-related serious clinical event (SCE) defined as any 1 of spinal cord compression, pathologic fracture, hypercalcaemia, uncontrolled local recurrence, brachial plexopathy, or poor functional status (Karnofsky performance score (KPS) ≤ 70) at the time of diagnosis of recurrence.			
	Secondary outcome: HRQoL as assessed using the MOS SF-36 and HADS			
Funding	Supported by Grant No. 010413 from the Canadian Breast Cancer Research Alliance			
Notes	We contacted study authors in October 2017 for information regarding final scores for SF-36 and HADS. Study authors replied with the relevant means and standard deviations.			



### Grunfeld 2006 (Continued)

### Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The Ontario Clinical Oncology Group. Randomization was conducted using a computer-generated center-specific schedule."
Allocation concealment (selection bias)	Low risk	Quote: "After patients provided informed consent, they were randomly allocated to treatment groups by a telephone call to the trial coordinating center of the Ontario Clinical Oncology Group."
Blinding of participants and personnel (perfor- mance bias) Objective outcomes	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.
Blinding of participants and personnel (perfor- mance bias) Patient-reported out- comes	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.
Blinding of outcome as- sessment (detection bias) Time-to-detection of re- currence	Low risk	The primary outcome (serious clinical event) was assessed by a committee that was blinded to treatment allocation.
Blinding of outcome as- sessment (detection bias) Patient-reported out- comes	Unclear risk	Participants were self-assessors and were not blinded but the likely direction of bias cannot be predicted.
Incomplete outcome data (attrition bias) Objective outcomes	Low risk	Similar reasons and number of withdrawals and exclusions in each group. All available data were included without imputation
Incomplete outcome data (attrition bias) Patient-reported out- comes	Low risk	Numbers for loss to follow-up were similar in both groups, although slightly more participants missed completion of SF-36 in the GP group at 12 months (414 vs 426). All available data were included without imputation.
Selective reporting (re- porting bias)	Low risk	All outcomes mentioned in the clinical trials protocol have been reported except for economic evaluation.
Other bias	Unclear risk	We detected no other bias

# **Grunfeld 2011**

Methods	Randomised trial
	SCP vs no SCP
	Cancer site: breast cancer
	Setting: 9 tertiary care cancer centres throughout Canada
	Accrual: April 2007-July 2009



Grunfeld 2011 (Continued)	Duration of follow-up:	2 years	
Participants 408 women with early stage breast cancer who ously		stage breast cancer who completed primary treatment at least 3 months previ-	
	-	ention: 61.2 (10.4) years; Control: 61.7 (10.2) years	
Interventions	Intervention group:     Comparison group:		
	• Comparison group: PCP with no SCP, n = 208  "All routine follow-up was transferred to the PCP. Patients had a standard discharge visit with the oncologist, and a discharge letter was sent to the PCP, which was consistent with usual practice. There was an instruction to PCPs to refer patients back to the oncologist if a recurrence or new primary cancer developed and an instruction both to patients and PCPs to schedule the first follow-up visit in approximately 3 months (all subsequent visits were arranged between the patient and PCP).		
	scribed elements, inclu tional follow-up guidel resource kit tailored to	ntion group additionally received a comprehensive SCP that consisted of the pre- uding a personalized treatment summary, a patient version of the Canadian na- ine, a summary table of the guideline that served as a reminder system, and a the patient's needs on available supportive care resources. These documents der and were reviewed with the patient during a 30-minute educational session	
Outcomes	Participant-reported outcomes were used to measure the domains of cancer-specific distress (IES); general psychological distress (POMS); HRQoL (SF-36 PCS and MCS); participant satisfaction (MOS-PSQ); continuity/co-ordination of care. Costs		
Funding	Supported by grant No. 17423 from the Canadian Breast Cancer Research Alliance, and by a clinician scientist award from the Ontario Institute for Cancer Research with funds from the Ontario Ministry of Research and Innovation (E.G.)		
Notes	We contacted study authors in October 2017 for information regarding final scores for SF-36 and HADS. Study authors replied with the relevant means and SDs.		
Risk of bias			
Bias	Authors' judgement	Support for judgement	
Random sequence generation (selection bias)	Low risk	Quote: "Eligible patients were allocated according to a prescribed computer-generated center and stratum-specific randomization schedule in a 1:1 ratio to either the intervention or control group."	
Allocation concealment (selection bias)	Low risk	Quote: "Concealed allocation was performed by contacting the trial coordination center of the Ontario Clinical Oncology Group by telephone."	
Blinding of participants and personnel (perfor- mance bias) Patient-reported out- comes	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.	
Blinding of outcome assessment (detection bias) Patient-reported outcomes	Unclear risk	Participants were self-assessors and were not blinded but the likely direction of bias cannot be predicted.	
Incomplete outcome data (attrition bias)	Low risk	Similar response rates in both groups.	



**Grunfeld 2011** (Continued)
Patient-reported outcomes

Selective reporting (reporting bias)	Unclear risk	No protocol available, however all outcomes mentioned in the aims were reported
Other bias	Unclear risk	We detected no other bias.

### Hershman 2013

Methods	Randomised trial		
	Addition of in-person SCP vs no SCP		
	Cancer site: breast cancer		
	Setting: Columbia University Medical Center, USA		
	Accrual: February 2008-June 2011		
	Duration of follow-up: 6 months		
Participants	141 women who had a history of stage 0–III breast cancer and were within 6 weeks of completion of initial adjuvant treatment (radiation or chemotherapy)		
	Age (mean): intervention: 54 years; control: 55 years		
Interventions	Intervention group: SCP, n = 71		
	• Comparison group: control group, n = 70		
	"Both groups were given the National Cancer Institute (NCI) publication, Facing Forward: Life after Cancer Treatment, by the research staff. Facing Forward is a guide for people who were treated for cancer. It is a 24-page manual, available in English and Spanish, that summarizes many key issues of interest to cancer survivors during the re-entry phase, and contains sections on a number of issues after cancer treatment, including medical care, potential symptoms, emotions, social relationships, and dealing with practical matters, such as insurance and employment.		
	The SCP group also met in person for about 1 hour with a nurse practitioner and a nutritionist (in English or Spanish) to receive a personalized treatment summary, surveillance recommendations, discussion of risk for late effects and toxicities, and screening and lifestyle recommendations. The content of the visit was based on guidelines from the American Society of Clinical Oncology (http://www.cancer.net/survivorship/asco-cancertreatment-summaries, http://preventcancer.aicr.org)."		
Outcomes	Treatment satisfaction, impact of cancer, survivorship concerns, physical and functional well-being subscales of the FACT, depression (CES-D) scale, health literacy, and symptoms assessment to capture treatment-related side effects		
Funding	Supported by a grant from Susan G. Komen for The Cure (DISP0706868). Additional funding provided from the Breast Cancer Research Foundation.		
Notes	This study did not provide the required data for inclusion in the meta-analyses.		
Risk of bias			
Bias	Authors' judgement Support for judgement		



Hershman 2013 (Continued)		
Random sequence generation (selection bias)	Low risk	Quote: "A block randomization list was created via a computer generated sequence for each of the stratification groups, and consent forms corresponding to the randomization arms were placed in sealed sequential envelopes."
Allocation concealment (selection bias)	Low risk	Quote: "The research staff was unaware of the randomization sequence."
Blinding of participants and personnel (perfor- mance bias) Patient-reported out- comes	Low risk	Quote: "Because the study posed minimal risk, subjects were told that they were in a study of cancer survivors and were unaware they were being randomized."
Blinding of outcome assessment (detection bias) Patient-reported outcomes	Low risk	Participants were self-assessors and were blinded.
Incomplete outcome data (attrition bias) Patient-reported outcomes	Low risk	Similar numbers and reasons for loss to follow-up and similar response rates in both groups
Selective reporting (reporting bias)	Unclear risk	No protocol available, however all outcomes mentioned in the aims were reported
Other bias	Unclear risk	We detected no other bias.

## Jefford 2016

Methods	Randomised trial		
	Addition of SCP vs usual care		
	Cancer site: colorectal cancer		
	Setting: 18 sites across 3 states in Australia in major metropolitan, regional, and rural areas in both public and private settings		
	Accrual: not reported		
	Duration of follow-up: 6 months		
Participants	221 patients with colon or rectal cancer stage I, II, or III and being treated with curative intent with surgery with or without radiation or chemotherapy		
	Age (mean/SD): intervention: 62.1 (11.4) years; usual care 63.1 (12) years		
	Sex: intervention: 52.3% men, 47.7% women; usual care: 50.9% men, 49.1% women		
Interventions	Intervention group: SCP group, n = 110		
	"SurvivorCare was added to usual post-treatment care and comprised the provision of survivorship educational materials, a tailored survivorship care plan, an individually tailored nurse face-to-face end of treatment consultation and three subsequent telephone calls."		
	• Comparison group: usual care, n = 111		



Jefford 2016 (Continued)		d to usual care will receive care according to the treating centre/practitioner's ments of the intervention will not be provided in the control group."
Outcomes	Depression (BSI-18), HRQoL (CaSUN, EORTC QLQ C-30), perceptions of post-treatment care (assessed with a survey developed specifically for this study)	
Funding	This study was funded jointly by the Victorian State Government through the Victorian Cancer Agency and by beyondblue, and the Australian Government through Cancer Australia, and was awarded through the Priority-driven Collaborative Cancer Research Scheme (Grant 628581).	
Notes	This study did not prov	vide the required data for inclusion in the meta-analyses.
	Possible conflicts of in	terests: CSL Limited and Mundipharma
Risk of bias		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Allocation was balanced by site using a minimization method and participants were randomly assigned and notified of allocation after completion of consent and baseline questionnaires."
Allocation concealment (selection bias)	Unclear risk	Allocation concealment was not reported.
Blinding of participants and personnel (perfor- mance bias) Patient-reported out- comes	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.
Blinding of outcome assessment (detection bias) Patient-reported outcomes	Unclear risk	Participants were self-assessors and were not blinded but the likely direction of bias cannot be predicted.
Incomplete outcome data (attrition bias) Patient-reported out- comes	Low risk	Similar numbers and reasons for loss to follow-up in both groups
Selective reporting (reporting bias)	Low risk	The study reports results on all outcomes described in the protocol
Other bias	Unclear risk	We detected no other bias

## Jeppesen 2018

Methods	Randomised trial
	Patient-initiated vs conventional specialist (standard hospital) follow-up
	Cancer site: endometrial cancer
	Setting: 4 Danish departments of gynaecology: Odense University Hospital, Aalborg University Hospital, Roskilde Hospital and Aarhus University Hospital
	Accrual: May 2013-May 2016



and personnel (perfor-

Patient-reported out-

Blinding of outcome as-

sessment (detection bias)

mance bias)

comes

Jeppesen 2018 (Continued)	Duration of follow-up: 3 years			
Participants	214 women treated with curative intent for FIGO stage I, grades 1 and 2 endometrial carcinoma			
	Age (mean/SD): interve	ention arm: 63.4 (8.3) years; comparison arm: 66.5 (8.9) years		
	Sex: 100% female			
Interventions	Intervention group:	participant-initiated follow-up, n = 105		
	"There was no scheduled of examinations at the respective department of gynaecology. The women were thoroughly instructed in alarm symptoms that required examination, that is vaginal bleeding/discharge or other newly emerged symptoms including: pelvic pain/heaviness, distended abdomen, dyspnoea, gastrointestinal symptoms, fatigue, weight loss and swelling of the leg(s). This information was provided verbally by a doctor specialised in gynaecological oncology immediately after randomisation. If they felt worried about the risk of recurrence, they could ask for a consultation. Self-referral was made easy by providing the telephone number of a designated project nurse at the department of gynaecology or, if preferred, they could contact their GP. In most cases, the women were seen within a week after contacting the department. The woman's GP was informed of the study and the woman's allocation through the discharge summary."			
	"Women in the control group received conventional follow up care, in accordance with Danish guide- lines. This was a 3-year follow-up period, consisting of scheduled visits every 4–6 months in the first 2 years and every 6 months during the third year. Because of the pragmatic study approach, variation in the frequency of follow-up visits was allowed, as each of the four centres was instructed to provide care as usual. The follow-up visits included clinical and gynaecological examinations with vaginal ultra- sound, supplemented with biopsies in case of suspicious findings and imaging in case of symptoms or histologically verified recurrence."			
Outcomes	Primary end point: fear of cancer recurrence after 10 months of follow-up (FCRI).			
	Additional end points (not yet published): QoL, unmet needs, and post-traumatic gromonths			
Funding	Funding from the Danish Cancer Society; National Research Centre for Cancer Rehabilitation, University of Southern Denmark; Region of Southern Denmark; Odense University Hospital			
Notes				
Risk of bias				
Bias	Authors' judgement	Support for judgement		
Random sequence generation (selection bias)	Low risk	Quote: "The women were randomly assigned (1:1) using a computer-based system stratified according to healthcare centre."		
Allocation concealment (selection bias)	Low risk	Quote: "Healthcare providers and data analysts were blinded during recruitment."		
Blinding of participants	Unclear risk	Given the nature of the study, it was not possible to blind participants or per-		

Unclear risk

sonnel.

Participants were self-assessors and were not blinded but the likely direction

assignment until all the analyses were completed.

of bias cannot be predicted. However, data analysts were blinded to the group



Jeppesen 2018	(Continued)
Patient-reporte	ed out-
comes	

comes		
Incomplete outcome data (attrition bias) Patient-reported out- comes	Low risk	Similar numbers lost to follow-up (26 in intervention arm and 30 in control arm) and no evidence of a difference was found in baseline and disease characteristics between responders and non-responders.
Selective reporting (reporting bias)	Low risk	The trial was registered on clinicaltrials.gov and all the pre-specified outcomes were mentioned in the article. However, only results for the primary outcome (fear of cancer recurrence) was published. Also, the article only mentions that cost analysis will be conducted at 3 years' follow-up while the clinical trial entry also states 34-month follow-up on all outcomes.
Other bias	Unclear risk	1. The 2 groups differed at baseline on the outcome of FCRI but no P value was reported. However analyses were adjusted for baseline scores.
		2. The baseline questionnaire was completed after randomisation. Responses could thus be affected by the allocation but the direction of bias is unclear.

### Juarez 2013

Methods	Randomised trial		
	Addition of NuevaLuz package vs usual care		
	Cancer site: breast cancer		
	Setting: hospital care clinic, USA		
	Accrual: not reported		
	Duration of follow-up: 6 months		
Participants	52 English and Spanish speaking Latinas ≥ 18 years with stage I, II, or III breast cancer and completed primary treatment		
	Age (mean/SD): 50.9 (9.2) years		
Interventions	Intervention group: Nueva Luz , n = 32		
	"Nueva Luz is an individualized, multidimensional bilingual (English/Spanish) QOL program designed to provide Latinas with breast cancer with structured information that was linguistically and culturally appropriate about high incidence QOL concerns and strategies to assist women transition into the survivorship period. Four weekly sessions of approximately 40- 60 minutes in length was provided. In addition to the intervention, participants received a bilingual education packet in a notebook format. Upon completion of the four sessions, monthly support through telephone-follow-up sessions was provided by the principal investigator."		
	• Comparison group: usual care, n = 18		

"Subjects randomized to the attention control group received initial face-to-face baseline assessment and completed questionnaires at baseline, 3 months and 6 months. They also received monthly telephone follow-up by the principal investigator. These phone calls were designed for retention purposes only. At the end of the 6-month study period, patients randomized to the attention control group were offered the education intervention delivered over 2 face-to-face sessions and bilingual printed teaching

materials were provided."



Juarez 2013 (Continued)		
Outcomes	The City of Hope Quality of Life Breast Cancer questionnaire, the Mishel Uncertainty in Illness Scale-Community, the Psychological Distress Thermometer	
Funding	The project described was supported by Grant Number K07CA106551-01A2 from the National Cancer Institute.	
Notes	This study did not provide the required data for inclusion in the meta analyses.	
Risk of bias		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (perfor- mance bias) Patient-reported out- comes	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.
Blinding of outcome assessment (detection bias) Patient-reported outcomes	Unclear risk	Participants were self-assessors and were not blinded but the likely direction of bias cannot be predicted.
Incomplete outcome data (attrition bias) Patient-reported out- comes	High risk	Quote: "Thirty- two experimental and 18 control patients were available for testing at all three time periods for most of these outcome variables (two experimental patients having been lost to follow- up at time 3)."  Comment: it is unclear why the groups were so dissimilar in size after randomisation even though the loss of only 2 participants may be considered low.
Selective reporting (reporting bias)	Unclear risk	No protocol available. However they do report on all the outcomes mentioned in the aims.
Other bias	High risk	The principal investigator was responsible for all aspects of study procedures, including participant accrual, obtaining informed consent, intervention implementation and follow-up for both the experimental and attention control groups. Furthermore, the 2 groups were highly imbalanced.

### Kimman 2011

Methods Randomised trial, 2 x 2 design

- 1) Nurse-led vs conventional specialist (hospital) follow-up
- 2) Educational programme vs no educational programme (not included in this review)

Cancer site: breast cancer

Setting: 7 hospitals and 2 radiotherapy clinics in the south of the Netherlands

Accrual: June 2005-March 2008



Kimman 2011 (Continued)	Duration of follow-up:	18 months		
Participants	320 women who had completed curative breast cancer treatment < 6 weeks prior to randomisation, with a WHO performance score between 0 and 2			
	Age (mean/SD): 55.8 (9.9) years			
Interventions	Comparison 1			
	• Intervention group: nurse-led telephone follow-up, n = 162			
	"A mammography at 12 months combined with an outpatient clinic visit, and telephone interviews by a breast care nurse (BCN) at the same time points as for the usual follow-up (i.e. 3, 6, 9 and 18 months)"			
	Comparison group:	hospital follow-up, n = 158		
	Five outpatient clinic visits in the first 18 months (at 3, 6, 9, 12 and 18 months), including a mammography at 12 months			
	Comparison 2			
	• Intervention group: follow-up (nurse-led or hospital) with educational group programme (EGP), n = 156			
	• Comparison group: follow-up with no EGP, n = 164			
	"The EGP consisted of two interactive group sessions of 2.5 h each and was attended by the patient +/-her partner within three months after treatment. The BCN provided information on possible treatment side-effects, signs and symptoms of a possible recurrence, prostheses and fatigue.			
	A health care psychologist addressed psychological and social consequences of breast cancer, particularly anxiety, depression, changes in family and social role patterns and discussed psychological coping strategies."			
Outcomes	Primary outcome for both interventions HRQoL, (EORTC QLQC30)			
	Secondary outcomes: emotional and role functioning (EORTC QLQ-C30 subscales), anxiety (STAI) and perceived feelings of control (Mastery Scale)			
	Details on the number of visits to the hospital, telephone contacts with medical specialists and breast-care nurses, as well as GP visits were collected using patient records and cost diaries			
Funding	This research was funded by the Netherlands Organisation for Health Research and Development (Grant No. 945- 04-512).			
Notes	We contacted study authors in September 2017 for information regarding which STAI subscale was used. Study author replied that the State subscale was used. We only included the results for the nurse led vs hospital comparison in this review to address issues regarding unit of analysis.			
Risk of bias				
Bias	Authors' judgement	Support for judgement		
Random sequence generation (selection bias)	Low risk	Quote: "Randomization by minimization was performed by the independent Comprehensive Cancer Center Limburg using a computerized randomization program (ALEA)."		
Allocation concealment (selection bias)	Low risk	Quote: "Randomisation by minimisation 14 was performed by the independent Comprehensive Cancer Centre Limburg using a computerised randomisation programme (ALEA)."		



Kimman 2011 (Continued)		
Blinding of participants and personnel (perfor- mance bias) Patient-reported out- comes	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.
Blinding of outcome assessment (detection bias) Patient-reported outcomes	Unclear risk	Participants were self-assessors and were not blinded but the likely direction of bias cannot be predicted.
Incomplete outcome data (attrition bias) Patient-reported out- comes	Low risk	Similar numbers and reasons for loss to follow-up and similar response rates in both groups
Selective reporting (reporting bias)	Low risk	Protocol available and all outcomes described in the protocol have been reported
Other bias	Unclear risk	We detected no other bias.

### Kirshbaum 2017

Methods	Randomised trial		
	Open access (patient-initiated) vs conventional specialist (standard hospital) follow-up		
	Cancer site: breast cancer		
	Setting: UK		
	Accrual: not reported		
	Duration of follow-up: 24 months		
Participants	112 women with AJCC Stage 1 or Stage 2 breast cancer, treated with curative intent		
	Age (mean/SD): intervention: 60.7 (10.86) years; control: 60.5 (9.79) years		
Interventions	<ul> <li>Intervention group: open-access follow-up, n = 56</li> <li>Comparison group: standard hospital follow-up, n = 56</li> </ul>		
	"All women attended a psycho-educational self-management programme designed by the UK charity Breast Cancer Care called "Living with Breast Cancer" (now known as "Moving Forward"). This comprised half-day sessions delivered over four consecutive weeks and addressed topics that included the management of breast cancer, the impact of breast cancer, breast reconstruction, lymphoedema, exercise, breast awareness after surgery, healthy eating and the management of menopausal symptoms.		
	Following attendance on the course, women were randomised into one of two groups: Women in the intervention group were not routinely followed-up. They were provided with a resource pack designed to complement the course and details of how to access breast surgical services through a telephone helpline run by breast cancer nurses should they experience any breast cancer related concerns. The comparison group was allocated to standard care hospital follow up."		
Outcomes	QoL QLQC30 and EORTC QLQ-BR23 and HADS		
Funding	Yorkshire Cancer Network; Breast Cancer Care; University of Bradford; Huddersfield University; Calderdale and Huddersfield NHS Trust		



### Kirshbaum 2017 (Continued)

Notes

Risk (	of bias
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Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Following attendance on the course, women were randomised into one of two groups: (1) standard hospital after- care (Control Group) and (2) open access after- care (Intervention Group)."
		Comment: sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	Allocation concealment not reported
Blinding of participants and personnel (perfor- mance bias) Patient-reported out- comes	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.
Blinding of outcome assessment (detection bias) Patient-reported outcomes	Unclear risk	Participants were self-assessors and were not blinded but the likely direction of bias cannot be predicted.
Incomplete outcome data (attrition bias) Patient-reported out- comes	Unclear risk	No information reported on reasons for loss to follow-up or if the attrition was equally distributed between the groups
Selective reporting (reporting bias)	Unclear risk	No protocol available, however all outcomes mentioned in the aims were reported
Other bias	Unclear risk	The only baseline characteristics reported were age and there seemed to be no differences between groups.

# Kjeldsen 1997

Methods	Randomised trial  More frequent vs less frequent follow-up		
	Cancer site: colorectal cancer		
	Setting: Odense University Hospital, Denmark		
	Accrual: January 1983-June 1994  Duration of follow-up: 180 months		
Participants	597 patients < 76 years treated with radical surgery for colorectal cancer		
	Age: not reported		
	Sex: more frequent group: 58% men, 42% women; less frequent group: 51% men, 49% women		
Interventions	• Intervention group: more frequent follow-up, n = 290		



#### Kjeldsen 1997 (Continued)

"Follow-up examinations at 6, 12, 18, 24, 30, 36, 48, 60, 120, 150 and 180 months after radical surgery. The examinations included medical history, clinical examination, digital rectal examination, gynaecological examination, Haemoccult-11 test (SmithKline Diagnostics, San Josc, California, USA), colonoscopy, chest radiograph, haemoglobin level, erythrocyte sedimentation rate and liver enzymes. Whenever recurrence was suspected, more detailed examinations were performed to detect possible treatable recurrence."

• Comparison group: less frequent follow-up, n = 307

"Examinations at 60, 120 and 180 months. The examinations included medical history, clinical examination, digital rectal examination, gynaecological examination, Haemoccult-11 test (SmithKline Diagnostics, San Josc, California, USA), colonoscopy, chest radiograph, haemoglobin level, erythrocyte sedimentation rate and liver enzymes. Whenever recurrence was suspected, more detailed examinations were performed to detect possible treatable recurrence."

Outcomes	Detection of recurrence and survival
Funding	This research was supported by The Danish Cancer Society.

## Notes

### Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "After surgery, the patients were allocated to one of two follow- up programmes (groups 1 and 2) by random numbers, stratified within the three Dukes stages."
		Comment: sequence generation was not reported.
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (perfor- mance bias) Objective outcomes	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.
Blinding of participants and personnel (perfor- mance bias) Patient-reported out- comes	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.
Blinding of outcome assessment (detection bias) Overall survival	Low risk	The outcome of survival is not likely to be biased.
Blinding of outcome assessment (detection bias) Time-to-detection of recurrence	Unclear risk	Assessors were not blinded and some of the clinical outcomes were based on judgements, but the likely direction of bias cannot be predicted.
Blinding of outcome assessment (detection bias) Patient-reported outcomes	Unclear risk	Participants were self-assessors and were not blinded, but the likely direction of bias cannot be predicted.



Kjeldsen 1997 (Continued)		
Incomplete outcome data (attrition bias) Objective outcomes	Low risk	Every participant appears to be followed-up.
Incomplete outcome data (attrition bias) Patient-reported out- comes	Low risk	Overall response rate was 91% and participants who left out individual items were contacted by phone and the missing information was obtained from all but 1 participant.
Selective reporting (reporting bias)	Unclear risk	No protocol available, however all outcomes mentioned in the aims were reported
Other bias	Unclear risk	We detected no other bias.

## **Koinberg 2004**

Methods	Randomised trial		
	On-demand (patient-initiated) vs conventional specialist (hospital) follow-up		
	Cancer site: breast cancer		
	Setting: hospital, Sweden		
	Accrual: 1991-2001		
	Duration of follow-up: 5 years		
Participants	264 women with a newly diagnosed breast cancer, classified as either p-TNM stage I or stage II		
	Age (mean/SD): nurse-led: 60 (10.3) years; standard hospital: 58.8 (10.1) years		
Interventions	Intervention group: nurse-led, on-demand follow-up, n = 133		
	"Initial meeting with specialized nurse 3 months after surgery. Information about how to recognise a recurrence in breast, skin, axilla and scar. Mammography at 1-year intervals and information about the result by telephone or letter. After 3 years, referral back to the routine mammography-screening programme. The nurse gave advice on aspects of self-care, such as medication and breast self examination and provided time for talking about the patient's psychosocial situation. The patient was requested to contact the nurse as soon as she had any questions or symptoms that she perceived could be related to breast cancer."		
	• Comparison group: standard hospital follow-up, n = 131		
	"A specialist in oncology or surgery examined the patients four times per year during the first 2 years after surgery, followed by bi-annual examinations for up to 5 years, and yearly after 5 years. At the follow-up visits, the examination included history taking concerning symptoms that could signal a loco-regional relapse or distant metastases as well as a clinical examination of the breasts, chest wall and regional lymph nodes. Mammography was carried out at 1-year intervals. Blood tests, chest X-ray or other imaging techniques were only performed on clinical indication."		
Outcomes	HADS, satisfaction and accessibility scale, time to recurrence and death, costs		
Funding	Not reported		
Notes	We contacted study authors in July 2018 for information on the log-rank P-value. No reply to date		
Risk of bias			



### Koinberg 2004 (Continued)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The random selection was computer-generated and stratified by centre."
Allocation concealment (selection bias)	Low risk	Quote: "Randomisation was achieved by means of telephone contact with an external secretariat. The random selection was computer-generated and stratified by centre. The block size was unknown to the study co-ordinators at the centres."
Blinding of participants and personnel (perfor- mance bias) Objective outcomes	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.
Blinding of participants and personnel (perfor- mance bias) Patient-reported out- comes	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.
Blinding of outcome assessment (detection bias) Overall survival	Low risk	The outcome of survival is not likely to be biased.
Blinding of outcome assessment (detection bias) Time-to-detection of recurrence	Unclear risk	Assessors were not blinded and some of the clinical outcomes were based on judgements, but the likely direction of bias cannot be predicted.
Blinding of outcome assessment (detection bias) Patient-reported outcomes	Unclear risk	Participants were self-assessors and were not blinded, but the likely direction of bias cannot be predicted.
Incomplete outcome data (attrition bias) Objective outcomes	Low risk	All participants appeared to be followed-up.
Incomplete outcome data (attrition bias) Patient-reported outcomes	Low risk	Response rates were high and similar in the 2 groups.
Selective reporting (reporting bias)	Unclear risk	No protocol available, however all outcomes mentioned in the aims were reported
Other bias	Unclear risk	We detected no other bias.

# Kokko 2003

Methods Randomised trial

Less intensive (CXR only when indicated) vs regular X-rays

Cancer site: breast cancer



Kokko 2003 (Continued)	Setting: Tampere Univ	ersity Hospital in Finland	
	Accrual: May 1991-Dec		
	-	5 years or 31 December 1999	
 Participants	472 with localised breast cancer (T1-4)		
·	Age (mean): 58 years		
Interventions	_	spontaneous arm, n = 229	
	"Patients had chest X-rays taken only when clinically indicated. During every visit a clinical examination of the patient was made by a physician and symptoms were asked using a patient questionnaire."		
	Comparison group: regular arm, n = 243		
		rays taken routinely every 6 months. During every visit a clinical examination of by a physician and symptoms were asked using a patient questionnaire."	
Outcomes	Sensitivity, specificity and predictive value of CXRs in detecting intrathoracic relapse as the first metastatic event, overall and disease-free survival, costs		
Funding	This study was financially supported by the Tampere University Hospital Research Foundation and the Finnish Breast Cancer Group.		
Notes	This study did not prov	vide the required data for inclusion in the meta-analyses.	
	We contacted study au	thors in July 2018 for information on the log-rank P value. No reply to date.	
Risk of bias			
Bias	Authors' judgement	Support for judgement	
Random sequence generation (selection bias)	Unclear risk	Quote: "The participants were randomized into the respective arms by simple random sampling."	
		Comment: Sequence generation not reported	
Allocation concealment (selection bias)	Unclear risk	Allocation concealment not reported	
Blinding of participants and personnel (perfor- mance bias) Objective outcomes	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.	
Blinding of outcome assessment (detection bias) Overall survival	Low risk	The outcome of survival is not likely to be biased.	
Blinding of outcome assessment (detection bias) Time-to-detection of recurrence	Unclear risk	Assessors were not blinded and some of the clinical outcomes were based on judgements, but the likely direction of bias cannot be predicted.	
Incomplete outcome data (attrition bias) Objective outcomes	Low risk	Quote: "No one was lost to follow-up."	



Kokko 2003 (Continued)		
Selective reporting (reporting bias)	Unclear risk	No protocol available, however all outcomes mentioned in the aims were reported
Other bias	Unclear risk	We detected no other bias.

### **Kvale 2016**

Allocation concealment

(selection bias)

Methods	Randomised trial  Addition of POSTCARE (SCP) intervention vs usual care only  Cancer site: breast cancer  Setting: hospital, USA		
	Accrual: not reported		
	Duration of follow-up: 3 months		
Participants	79 patients age ≥ 19 ye year of completing act	ears, diagnosed with non-metastatic cancer (AJCC TNM stage 0-IIIb) and within 1 ive cancer treatment.	
	Age (mean/SD): interve	ention: 57.23 (9.15) years; controls: 59.51 (11.96) years	
Interventions	Intervention group:	POSTCARE intervention, n = 40	
	niques to engage patie and strategies related On average, completio	rention is a single coaching encounter using motivational interviewing (MI) techents in the development of a patient-owned SCP that incorporates health goals to cancer follow-up, surveillance, symptom management, and health behavior. On of the session requires 75 minutes (range, 31-126 minutes). The survivorship was delivered by masters-level mental health professionals who completed MI usual care, n = 39	
	"The usual-care group provided baseline data and 3-month follow-up data. During the study period, routine care did not include the provision of a standardized treatment summary or SCP."		
Outcomes	SF-36, Social/Role Activities Limitations, Self-Efficacy for Managing Chronic Disease 6-Item Scale, the Patient Activation Measure–Short Form, and PHQ-9 depression scale at baseline and at 3-month follow-up		
Funding	Supported by the American Cancer Society (grant ACS121093- CCCDA-11-191-01-CCCDA)		
Notes	This study did not prov	vide the required data for inclusion in the meta-analyses.	
Risk of bias			
Bias	Authors' judgement	Support for judgement	
Random sequence generation (selection bias)	Low risk	Quote: "Participants were randomly assigned (1:1 randomization) using a permuted block design to the POSTCARE intervention or usual care."	
All II		0 1 110 111 1 1 1 1 1 1 1 1 1 1 1 1 1 1	

Quote: "Participants were randomly assigned (1:1 randomization) using a per-

muted block design to the POSTCARE intervention or usual care."

Comment: Whether allocation was concealed is not reported.

Unclear risk



Kvale 2016 (Continued)		
Blinding of participants and personnel (perfor- mance bias) Patient-reported out- comes	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.
Blinding of outcome assessment (detection bias) Patient-reported outcomes	Unclear risk	Participants were self-assessors and were not blinded, but the likely direction of bias cannot be predicted.
Incomplete outcome data (attrition bias) Patient-reported out- comes	Low risk	The CONSORT diagram shows similar numbers and reasons for attrition in both groups.
Selective reporting (reporting bias)	Unclear risk	No protocol available, however all outcomes mentioned in the aims were reported
Other bias	Unclear risk	We detected no other bias.

### Malmstrom 2016

Methods	Randomised trial		
	Addition of nurse-led telephone supportive care vs usual care		
	Cancer site: oesophageal cancer		
	Setting: university hospital in Sweden		
	Accrual: 2009-2013		
	Duration of follow-up: 6 months		
Participants	82 patients after oesophagectomy or oesophagogastrectomy for cancer in the oesophagus or cardia (C15, C16.0)		
	Age (mean): 66.4 years		
Interventions	<ul> <li>Intervention group: nurse-led telephone supportive care, n = 41</li> </ul>		
	"In addition to 'conventional care' the intervention group had a nurse led telephone supportive care programme. The intervention was provided by one nurse only, who was specialised on postoperative oesophageal cancer care. The intervention included a meeting before discharge where the patients had the opportunity to ask questions, discuss their concerns and received both oral and written information focusing on life after surgery, self-care, plans for the future, and where to turn to for help if needed. After discharge, the follow-up by the nurse was proactive and focused on the patients individual needs of support as well as areas known to be problematic for patients after this type of surgery e.g. nutrition, elimination, pain and psychological issues aiming to detect possible problems in an early stage and to help patients to manage them. The mean number of telephone contacts during the 6 month follow-up was 16 times. The telephone contacts lasted as long as the patients desired, and usually between 5 and 15 min."		
	• Comparison group: conventional care, n = 41		
	"Conventional care was based on a clinical follow-up programme including clinical visits to one of the operating surgeons, and with the possibility to contact a nurse, in the out-patient clinic if needed. Be-		

fore discharge, the patients received information from a nutritionist about diet and weight controls,



Malmstrom 2016 (Continued)	the nutritionist approx	apist about postoperative exercises. All patients had a telephone follow-up by imately one week after discharge and repeatedly based on the patients' needs, tion or proactive contacts were included in the conventional care follow-up pro-		
Outcomes	Overall QoL in particip	ants with cancer (EORTC QLQ-C30) and diagnosis-specific QO (QLQ-OG25).		
	Participants' experienc	ce of perceived level of information (QLQ-INFO25)		
	Self-administrated dia	ries were used to register the number of health care contacts after discharge.		
Funding		This study was supported by grants from Södra sjukvårdsregionen (The Southern Regional Health Care Committee) and Vårdakademin (Academy of caring science) at Skåne University		
Notes	This study did not prov	ride the required data for inclusion in the meta-analyses.		
Risk of bias				
Bias	Authors' judgement	Support for judgement		
Random sequence generation (selection bias)	Low risk	Quote: "Sealed envelope technique through a block randomisation (10 patients /block). The last block included 12 patients."		
Allocation concealment (selection bias)	Low risk	Quote: "Sealed envelope technique through a block randomisation (10 patients /block). The last block included 12 patients."		
Blinding of participants and personnel (perfor- mance bias) Patient-reported out- comes	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.		
Blinding of outcome assessment (detection bias) Patient-reported outcomes	Unclear risk	Participants were self-assessors and were not blinded but the likely direction of bias cannot be predicted.		
Incomplete outcome data (attrition bias) Patient-reported outcomes	Low risk	Non-response was initially higher in the control group from 2 weeks onwards although by the time of the 6-month follow-up response rates were similar. Reasons given by participants for not responding were the same for both groups.		
Selective reporting (reporting bias)	Unclear risk	No protocol available, however all outcomes mentioned in the aims were reported		
Other bias	Unclear risk	We detected no other bias.		

## Maly 2017

Methods	Randomised trial		
	Treatment summaries and SCPs (TSSP) vs usual care only		
	Cancer site: breast cancer		
	Setting: 2 public institutions in Los Angeles County, Harbor-University of California at Los Angeles (UCLA) Medical Center and Los Angeles County plus University of Southern California Medical Center, USA		



Maly 2017 (Continued)	Accrual: December 201	2- July 2014	
	Duration of follow-up:	·	
Participants	219 women with breas treatment at least 1 mo	t cancer stage 0, I, II, or III, 10-24 months earlier who had their last definitive onth earlier	
	Age (mean/range): TSS	P group 52.5 (29-85); usual care group 53.2 (31-76)	
Interventions	Intervention group:	TSSP group, n = 110	
	in-person counseling s were generated by a co plan but adapted for lo terview, the nurse sche at UCLA to review the 1 most involved with her TSSP to future visits wi	sed on the development and receipt of an individually tailored TSSP and one ession with a trained, bilingual, bicultural nurse to review the contents. TSSPs omputerized program that was based on the Journey Forward survivorship care ow-literacy and Spanish-speaking populations. One month after the baseline ineduled a 1-hour session with each intervention participant in a research office TSSP. Each woman was encouraged to make an appointment with the physician reancer care to discuss the TSSP and the question list, and to take a copy of her ith other providers. A cover letter and two copies of the TSSP were mailed to the nics at the two study sites to be scanned into or attached to the patients' medical	
	• Comparison group: usual care, n = 109		
	"Usual care was provided to the control-group participants who received their personalized TSSPs after the final study data collection."		
Outcomes	Primary outcome: physician implementation of specific recommendations for each survivorship care need identified for each participant at the baseline interview by participant report.  Secondary outcomes: participant adherence to recommended survivorship care up to the 12-month interview and scores on the SF-12 Health Survey, at baseline and 12 months, to assess physical and mental health change during the study		
Funding	Supported by National Institutes of Health, National Cancer Institute Grant No. 1R01CA140481-01A		
Notes	This study did not provide the required data for inclusion in the meta-analyses. The study author is retired and did not have the resources to provide the necessary data.		
	Possible conflicts of in	terest	
	trinsic LifeSciences (I), & Johnson, Pfizer, Glax visory Role: Keryx (I), N Funding: Keryx (I) Pate anemia of chronic dise	nt: Optum rship: Intrinsic LifeSciences (I) Stock or Other Ownership: Xenon Pharma (I), In-Silarus Therapeutics (I), Merganser Biotech (I), Teva, Novartis, Merck, Johnson coSmithKline, Abbott Laboratories Honoraria: Vifor Pharma (I) Consulting or Adderganser Biotech (I), Silarus Therapeutics (I), InformedDNA, Eli Lilly Research nts, Royalties, Other Intellectual Property: related to iron metabolism and the lase (I), Up-to-Date royalties for section editor on survivorship Travel, Accommoninsic LifeSciences (I), Keryx (I)	
Risk of bias			
Bias	Authors' judgement	Support for judgement	
Random sequence generation (selection bias)	Low risk	Quote: "Randomization occurred with a one-to-one allocation to intervention or control within each study site, using a permuted block design with a block size of 4 or 6."	
Allocation concealment (selection bias)	Low risk	Although not reported, we assume that allocation was concealed due to randomisation using permuted block design with a block size of 4 or 6.	



Maly 2017 (Continued)		
Blinding of participants and personnel (perfor- mance bias) Patient-reported out- comes	Unclear risk	Given the nature of the study blinding was not possible.
Blinding of outcome assessment (detection bias) Time-to-detection of recurrence	Unclear risk	Both interviewer and participants were blinded to allocation group at base- line. However, the interviewers were not blinded to treatment group at the 12- month interview because the intervention group participants were asked addi- tional intervention-specific questions.
Incomplete outcome data (attrition bias) Patient-reported outcomes	Low risk	There were similar response rates in both groups.
Selective reporting (reporting bias)	Unclear risk	Cost was reported as an outcome in the study entry at clinicaltrial.gov, but not reported in this paper.  Data for SF-12 after 12 months was only reported as: "no significant differences in improvement of SF-12 scores from baseline to 12 months between groups (data not shown)."
Other bias	Unclear risk	We detected no other bias.

## Monteil 2010

Methods	Randomised trial			
	More intensive (coincidence detection system imaging (CDET)) vs CT scans			
	Cancer site: NSCLC			
	Setting: hospital, France			
	Accrual: October 2000-December 2002			
	Duration of follow-up: minimum of 2 years			
Participants	69 patients with histologically confirmed resected NSCLC stages I, II or IIIA			
	Age (median/range): 62 (42-82) years			
Interventions	Intervention group: CDET, n = 36			
	"CDET was performed using a dual-detector gamma camera (Axis; Phillips Medical Systems, Cleveland, Ohio, USA) equipped with a 19-mm sodium iodine crystal with septa operating in coincidence mode for acquisition. Serum glucose was measured before radiotracer injection. CDET was performed 60 minutes post 18F-fluorodeoxyglucose (18-FDG) injection."			
	• Comparison group: no treatment change, n = 33			
	"Chest CT scan with liver and adrenal gland section, abdominal ultrasonography, and bone scintigraphy (only if bone symptoms) were performed. Spiral CT examinations were performed using high-speed acquisition (Lightspeed, GE Medical Systems, Waukesha, WI, USA).			
	In the two groups, brain CT was performed at each imaging evaluation. These two surveillance programs were systematically performed at 6, 12, 18 and 24 months or earlier if recurrence was suspected."			



Monteil 2010 (Continued)			
Outcomes		f the study was the number of recurrences or new tumours detected in sympto- c participants and disease-free and overall survival, cost analysis	
Funding	This work was supported by a grant from the University Hospital of Limoges (local clinical research program, 2000).		
Notes	This study did not prov	ride the required data for inclusion in the meta-analyses.	
Risk of bias			
Bias	Authors' judgement	Support for judgement	
Random sequence generation (selection bias)	Unclear risk	Quote: "On the first clinical visit one month after surgery, all the patients were blindly randomized between two follow-up procedures."	
		Comment: sequence generation was not reported.	
Allocation concealment (selection bias)	Unclear risk	Allocation concealment was not reported.	
Blinding of participants and personnel (perfor- mance bias) Objective outcomes	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.	
Blinding of outcome assessment (detection bias) Overall survival	Low risk	The outcome of survival is unlikely to be biased.	
Blinding of outcome assessment (detection bias) Time-to-detection of recurrence	Unclear risk	Assessors were not blinded and some of the clinical outcomes were based on judgements, but the likely direction of bias cannot be predicted.	
Incomplete outcome data (attrition bias) Objective outcomes	Unclear risk	Attrition was not reported.	
Selective reporting (reporting bias)	Low risk	All outcomes mentioned in the clinical trials entry were reported.	
Other bias	Unclear risk	We detected no other bias.	

### Morrison 2018

Methods	Randomised trial		
	Nurse-led telephone vs conventional specialist (hospital) follow-up		
	Cancer site: gynaecological (cervical, endometrial, epithelial ovarian or vulval cancer)		
	Setting: 3 hospitals in North Wales, UK		
	Accrual: September 2015-February 2016		
	Duration of follow-up: 6 months		



#### Morrison 2018 (Continued)

#### **Participants**

24 women who had completed treatment for cervical, endometrial, epithelial ovarian or vulval cancer within the last 3 months and in the view of the treating consultant had no need for continued hospital-based care

Age (mean/SD/range): intervention group: 59.5 (11.1); 40-75 years; hospital group: 60 (11.9); 42-77 years

#### Interventions

• Intervention group: nurse-led telephone follow-up, n = 12

"These participants did not attend the hospital for their follow-up appointments but instead received a scheduled nurse-led telephone follow-up, firstly within 4 weeks of randomization and again 6 months after baseline. Patients were asked to complete the needs assessment measures before each scheduled telephone call to inform a structured discussion with the CNS. Any issues identified in these calls were referred to the most appropriate source of help. Additional telephone calls could be instigated at any time by the patient, where her completed needs assessments would be discussed as with scheduled calls."

• Comparison group: hospital follow-up, n = 12

"Patients randomized to standard care continued to have their hospital-based, consultant-led medical reviews at 3 and 6 months after baseline and were followed up according to an agreed protocol with the regional gynecological cancer multidisciplinary team that represented current practice."

#### Outcomes

Primary outcomes assessed the feasibility of running a larger trial including participant eligibility, recruitment and retention rates and outcome measure completion.

Secondary outcomes were generic and HRQoL (EORTC QLQ-C30, EQ-5D-3L, ICECAP-A), and a participant self-report health service use, data collected at 3 time points (baseline, 3 and 6 months) and costs

#### Funding

The TOPCAT-G study was funded and sponsored by the Betsi Cadwaladr University Health Board (BCUHB), Ysbyty Gwynedd, Penrhosgarnedd, Bangor, LL57 2PZ

### Notes

This study did not provide the required data for inclusion in the meta-analyses.

### Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Participants were randomised on a 1:1 ratio by the North Wales Organisation for Randomised Trials in Health (NWORTH) using a dynamic, independent, secure, web-based, randomisation procedure."
Allocation concealment (selection bias)	Low risk	Quote: "Participants were randomised on a 1:1 ratio by the North Wales Organisation for Randomised Trials in Health (NWORTH) using a dynamic, independent, secure, web-based, randomisation procedure."
Blinding of participants and personnel (perfor- mance bias) Patient-reported out- comes	Unclear risk	Given the nature of the intervention, it was not possible to blind participants or personnel.
Blinding of outcome assessment (detection bias) Patient-reported outcomes	Unclear risk	Participants were self-assessors and were not blinded but the likely direction of bias cannot be predicted
Incomplete outcome data (attrition bias)	Low risk	Only 1 participant in the intervention group was lost to follow-up.



Morrison 2018 (Continued)
Patient-reported out-
comes

Selective reporting (reporting bias)	Low risk	The study protocol is available and pre-defined outcomes were reported.
Other bias	Unclear risk	The 2 groups differed at baseline: differences were noted at baseline between the 2 treatment allocations on several outcome measures, however analyses were adjusted for baseline scores.

## Murchie 2010

Methods	Randomised trial, open cluster design			
	GP-led vs conventional specialist (hospital) follow-up			
	Cancer site: cutaneous melanoma			
	Setting: a total of 35 general practices in north-east Scotland			
	Accrual: April 2005-April 2006			
	Duration of follow-up: 12 months			
Participants	142 patients diagnosed with and successfully treated for primary cutaneous malignant melanoma: ≤ 4 mm, diagnosed > 6 months but < 10 years previously or > 4 mm diagnosed > 3 years but < 10 years previously			
	Age (mean/SD): intervention group 58.7 (14.6) years; control group 59.5 (15.5) years			
	Sex: 51.4% women, 48.6% men			
Interventions	• Intervention group: GP-led, n = 53			
	"A lead GP from each of the intervention practices attended a 4-h training session and received a comprehensive information manual detailing how to deliver the study protocol for a 12-month period. This session focused on the presentation of new and recurrent melanomas and how best to examine to identify these. All patients in the intervention group received a detailed information booklet about melanoma, which included information on conducting self-examination. The intervention group patients were invited to attend scheduled protocol based melanoma follow-up appointments with the lead GP at their practice, at 3 or 6-monthly intervals depending on the thickness of melanoma and time since diagnosis. This schedule of visits is identical to that followed by the specialists running the Joint Melanoma Clinic at the ARI."			
	<ul> <li>Comparison group: traditional hospital follow-up, n = 89</li> </ul>			
	"The GPs at control practices received no training in melanoma follow-up and had no scheduled consultations with their patients as part of the study. Patients at practices randomised to the control group continued to attend the hospital-based joint melanoma clinic for their melanoma follow-up, at 3 or 6-monthly intervals depending on the thickness of melanoma and time since diagnosis."			
Outcomes	Participant satisfaction, adherence to local guidelines was determined in relation to the current locally recommended schedule from the hospital joint melanoma clinic, health status (SF-36) and anxiety and depression (HADS).			
Funding	This study was entirely funded by Cancer Research UK (Grant No. C10673/A3912). The University of Aberdeen acted as the sponsor for this study.			



### Murchie 2010 (Continued)

Notes

This study did not provide the required data for meta-analyses. We contacted study authors in October 2017 requesting means for SF-36 and HADS. No reply to date.

### Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Practices were then randomised within each stratum to intervention or control using the randomisation function of the computer software package SPSS version 15.0 (SPSS Inc., Chicago, IL, USA)."
Allocation concealment (selection bias)	Low risk	Quote: "Practices were then randomised within each stratum to intervention or control using the randomisation function of the computer software package SPSS version 15.0 (SPSS Inc., Chicago, IL, USA)."
Blinding of participants and personnel (perfor- mance bias) Patient-reported out- comes	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.
Blinding of outcome assessment (detection bias) Patient-reported outcomes	Unclear risk	Participants were self-assessors and were not blinded but the likely direction of bias cannot be predicted.
Incomplete outcome data (attrition bias) Objective outcomes	Low risk	Attrition and follow-up were similar in both groups.
Incomplete outcome data (attrition bias) Patient-reported out- comes	Low risk	Response rates were similar in both groups.
Selective reporting (reporting bias)	Unclear risk	No protocol available however all the outcomes mentioned in the aims were reported.
Other bias	High risk	Quote: "The imbalance in numbers was a result of lower recruitment than anticipated in several larger practices."
		Comment: The intervention group was much smaller than the control group.
		Quote: "According to the protocol, 22 members of the intervention group required a 3-monthly follow-up and 31 required a 6-monthly follow-up. As a result, the median number of GP-led melanoma follow-up appointments experienced by the intervention group was two. This may have limited their ability to make comparisons with their hospital follow-up."

### Mäkelä 1992

Methods

**Randomised trial** 

More intensive diagnostic procedures vs less intensive diagnostic procedures

Cancer site: colorectal cancer



Mäkelä 1992 (Continued)	Sotting: Ouls University	v. Hospital Finland		
	Setting: Oulu University Hospital, Finland			
	Accrual: 1988-1990	Fugars		
	Duration of follow-up: 5 years			
Participants		ough primary surgery for colorectal cancer		
	Age (mean/SD): intensi	ive group: 63 (15) years; less intensive group: 69 (15) years		
Interventions	• Intervention group:	intensified group, n = 52		
	"Colonoscopy with video-imaging 3 months after surgery, if not performed preoperatively, and thereafter once a year for all. Flexible fibresigmoidoscopy with video imaging every third month for patient who had been operated on for rectal or sigmoid tumours. Ultrasonography of the liver was not performed preoperatively, but it was performed every 6 months after operation and computed tomography (CT) of the liver and the site of primary resection every year after operation."			
	• Comparison group:	less intensive group, n = 54		
	"Rigid sigmoidoscopy was performed at each visit for patients who underwent surgery for rectal and sigmoid cancers and a barium enema for all patients at 12 months and then once per year."			
Outcomes	Time to detection of recurrence, the recurrence rates, the first method showing recurrence, the number, mode and site of the tumours, treatment of the recurrence, survival and the number of synchronous adenomas removed during follow-up			
Funding	Not reported			
Notes				
Risk of bias				
Bias	Authors' judgement	Support for judgement		
Random sequence generation (selection bias)	Unclear risk	Quote: "These patients were randomized during hospitalization into two follow-up programs: group 1, 54 patients (the old conventional follow-up program) and group 2, 52 patients (an intensified protocol)."		
		Comment: sequence generation was not reported.		
Allocation concealment (selection bias)	Unclear risk	Quote: "These patients were randomized during hospitalization into two follow-up programs: group 1, 54 patients (the old conventional follow-up program) and group 2, 52 patients (an intensified protocol)."		
		Comment: allocation concealment was not reported.		
Blinding of participants and personnel (perfor- mance bias) Objective outcomes	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.		
Blinding of outcome assessment (detection bias) Overall survival	Low risk	The outcome of survival is not likely to be biased.		
Blinding of outcome assessment (detection bias) Time-to-detection of recurrence	Unclear risk	Assessors were not blinded and some of the clinical outcomes were based on judgements, but the likely direction of bias cannot be predicted.		



Mäkelä 1992 (Continued)		
Incomplete outcome data (attrition bias) Objective outcomes	Low risk	All participants appeared to be followed-up.
Selective reporting (reporting bias)	Unclear risk	No protocol available, however all outcomes mentioned in the aims were reported.
Other bias	Unclear risk	We detected no other bias.

### Ohlsson 1995

Age (mean/range): intensive group: 65.7 (40.6-83.3) years; no fold Sex: 51 men, 56 women  Interventions  Intervention group: intensive group, n = 53  "Planned examinations 3, 6, 9, 12, 15, 18, 21, 24, 30, 36, 42, 48 an Physical examination, Rigid proctosigmoidoscopy, Blood tests, Rendoscopic control of the anastomosis at 9, 21 and 42 months.  Complete colonoscopy at 3, 15, 30 and 60 months.  Computed tomography of the pelvis at 3, 6, 12, 18, 24 months"  Comparison group: no follow-up group, n = 54  "No follow-up visits were planned for patients in the control group recommending they leave fecal samples with the district nurse for third month during the two first years after surgery and then one contact the surgical department as soon as they experienced and dominal or perineal pain, altered bowel movements, change in for weight loss."  Disease-free survival and 5-year survival rate				
Setting: hospitals in Lund and Helsingborg, Sweden Accrual: 1983-1986  Duration of follow-up: median follow-up time was 6.8 (range 5.5.)  Participants  107 participants undergoing resection with curative intent for concept (age) (mean/range): intensive group: 65.7 (40.6-83.3) years; no follow-up: intensive group, n = 53  "Planned examinations 3, 6, 9, 12, 15, 18, 21, 24, 30, 36, 42, 48 and Physical examination, Rigid proctosigmoidoscopy, Blood tests, for Endoscopic control of the anastomosis at 9, 21 and 42 months.  Complete colonoscopy at 3, 15, 30 and 60 months.  Computed tomography of the pelvis at 3, 6, 12, 18, 24 months"  • Comparison group: no follow-up group, n = 54  "No follow-up visits were planned for patients in the control group recommending they leave fecal samples with the district nurse for third month during the two first years after surgery and then one contact the surgical department as soon as they experienced and dominal or perineal pain, altered bowel movements, change in following the surgical department as soon as they experienced and dominal or perineal pain, altered bowel movements, change in following the surgical department as soon as they experienced and dominal or perineal pain, altered bowel movements, change in following the surgical department as soon as they experienced and dominal or perineal pain, altered bowel movements, change in following the surgical department as soon as the surgical and dominal or perineal pain, altered bowel movements, change in following the surgical department as soon as				
Accrual: 1983-1986  Duration of follow-up: median follow-up time was 6.8 (range 5.5)  Participants  107 participants undergoing resection with curative intent for concept Age (mean/range): intensive group: 65.7 (40.6-83.3) years; no follows: 51 men, 56 women  Interventions  • Intervention group: intensive group, n = 53  "Planned examinations 3, 6, 9, 12, 15, 18, 21, 24, 30, 36, 42, 48 and Physical examination, Rigid proctosigmoidoscopy, Blood tests, for Endoscopic control of the anastomosis at 9, 21 and 42 months.  Complete colonoscopy at 3, 15, 30 and 60 months.  Computed tomography of the pelvis at 3, 6, 12, 18, 24 months"  • Comparison group: no follow-up group, n = 54  "No follow-up visits were planned for patients in the control group recommending they leave fecal samples with the district nurse for third month during the two first years after surgery and then oncontact the surgical department as soon as they experienced and dominal or perineal pain, altered bowel movements, change in for weight loss."  Outcomes  Disease-free survival and 5-year survival rate  Funding  Supported by grants from Lund University and the Swedish Med B93-17X-07183-09A)				
Duration of follow-up: median follow-up time was 6.8 (range 5.5.)  Participants 107 participants undergoing resection with curative intent for contact Age (mean/range): intensive group: 65.7 (40.6-83.3) years; no follows: 51 men, 56 women  Interventions • Intervention group: intensive group, n = 53  "Planned examinations 3, 6, 9, 12, 15, 18, 21, 24, 30, 36, 42, 48 and Physical examination, Rigid proctosigmoidoscopy, Blood tests, for Endoscopic control of the anastomosis at 9, 21 and 42 months.  Complete colonoscopy at 3, 15, 30 and 60 months.  Computed tomography of the pelvis at 3, 6, 12, 18, 24 months"  • Comparison group: no follow-up group, n = 54  "No follow-up visits were planned for patients in the control group recommending they leave fecal samples with the district nurse for third month during the two first years after surgery and then one contact the surgical department as soon as they experienced and dominal or perineal pain, altered bowel movements, change in form weight loss."  Outcomes  Disease-free survival and 5-year survival rate  Funding  Supported by grants from Lund University and the Swedish Med B93-17X-07183-09A)				
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B93-17X-07183-09A) Notes				
	Supported by grants from Lund University and the Swedish Medical Research Council (Grant B93-17X-07183-09A)			
Risk of bias				
Bias Authors' judgement Support for judgement				



Ohlsson 1995 (Continued)		
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients with other neoplastic polyps (eight patients in the control group and six in the F-U group) were randomized after removal of the polyps."
		Comment: sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	Allocation concealment not reported
Blinding of participants and personnel (perfor- mance bias) Objective outcomes	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.
Blinding of outcome assessment (detection bias) Overall survival	Low risk	The outcome of survival is not likely to be biased.
Blinding of outcome assessment (detection bias) Time-to-detection of recurrence	Unclear risk	Assessors were not blinded and some of the clinical outcomes were based on judgements, but the likely direction of bias cannot be predicted.
Incomplete outcome data (attrition bias) Objective outcomes	Low risk	All participants appear to be followed up for recurrences or death
Selective reporting (reporting bias)	Unclear risk	No protocol available, however all the outcomes mentioned in the aims were reported.
Other bias	Unclear risk	Baseline characteristics was not described in the text but data were presented in a table and there appeared to be differences in baseline characteristics with regard to gender. However, the likely direction of bias is difficult to predict.

### **Oltra 2007**

Randomised trial		
More intensive (additional diagnostic tests) vs standard follow-up		
Cancer site: breast cancer		
Setting: Hospital Universitari la Fe, Valencia, Spain		
Accrual: January 1997–December 1999		
Duration of follow-up: not reported but appointments were scheduled over 5 years		
121 women having been diagnosed as having breast cancer at stages I, II, or III and who had completed an initial curative treatment		
Age: not reported		
Intervention group: intensive group, n = 58		
"In the intensive follow-up arm, in addition to the anamnesis and physical examination, biochemistry, hematogram, and the markers carcinoembryonic antigen (CEA) and CA15.3 were assessed at every outpatient visit together with an annual hepatic echography, chest x-ray, and bone scan. All patients, irrespective of their group assignment, had annual mammography."		



0	ltra	200	(Continued)
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• Comparison group: standard follow-up group, n = 63

"In the standard clinical follow-up arm, the patients had a careful history and physical examination; no complementary tests were undertaken if the clinical symptoms at the time did not require them. All patients, irrespective of their group assignment, had annual mammography."

Outcomes	Relapses and overall costs of follow-up	
Funding	Not reported	
Notes	This study did not provide the required data for inclusion in the meta-analyses.	

#### Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Those who provided written informed consent to participation were randomly assigned to one of the follow-up arms of the study."
		Comment: sequence generation is not described.
Allocation concealment (selection bias)	Unclear risk	Allocation concealment was not reported.
Blinding of participants and personnel (perfor- mance bias) Objective outcomes	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.
Blinding of outcome assessment (detection bias) Time-to-detection of recurrence	Unclear risk	Assessors were not blinded and as some of the clinical outcomes were based on judgements, the likely direction of bias cannot be predicted.
Incomplete outcome data (attrition bias) Objective outcomes	Low risk	In both groups, similar numbers of participants were lost to follow-up. Reasons were not reported, but the numbers were very small.
Selective reporting (reporting bias)	Unclear risk	No protocol available, however all the outcomes mentioned in the aims were reported.
Other bias	Unclear risk	Baseline characteristics was not described in the text but data was presented in a table and there appears to be baseline differences with regards to disease stages I and IIA. However, the likely direction of bias is difficult to predict.

### Picardi 2014

Methods Randomised trial

Less intensive (US/chest radiography) vs standard (PET/CT scans)

Cancer site: HL

Setting: hospital, Italy

Accrual: June 2001-December 2009

Duration of follow-up: median follow-up of 60 months



#### Picardi 2014 (Continued)

#### **Participants**

300 participants with histologically proven HL, Ann Arbor or Cotswold stage ≥ IIB with bulky disease and/or extranodal lesions or stages III–IV, and achievement of complete response confirmed at FDG PET after first-line treatment.

Age (median/range): US/chest radiography: 29 years (18-70); PET/CT: 29 years (18-70)

Sex: US/chest radiography: 40% female, 60% male; PET/CT: 39% female; 61% male

#### Interventions

• Intervention group: US/chest radiography, n = 150

"Follow-up imaging procedures in the US/chest radiography group comprised US imaging for the evaluation of superficial, anterosuperior mediastinal, abdominal, and pelvic lymph nodes, and frontal and lateral chest radiography for the evaluation of mediastinal compartments. Each complete examination required an average of 40 minutes (range, 30–60 minutes)."

Comparison group: PET/CT, n = 150

"In the PET/CT group, total-body FDG PET/CT imaging was performed by using a combined in-line system (Discovery LS; GE Medical Systems, Milwaukee, Wis). Each examination included a unenhanced low-dose (80 mAs) four detector–row spiral CT scan, immediately followed by PET of the same field of view as that of the CT, according to a protocol reported in detail elsewhere. A dose of 5.3 MBq/kg 6 1 of FDG was injected intravenously 60 minutes 6 10 before imaging. PET scans were performed from the midbrain to the upper thigh after an 8-hour fast, with two-dimensional emission scans of 4 minutes per bed position."

#### Outcomes

Sensitivity for diagnosis of HL recurrence for each of the 2 follow-up imaging approaches, specificity, positive and negative predictive value, time of recurrence detection, and estimation of dose of ionising radiation and costs.

### Funding

Supported by the Associazione Italiana contro le Leucemie (Napoli Section)

### Notes

We contacted study authors in July 2018 for information on the log-rank P value. Study authors provided the hazard ratio with the associated confidence intervals and log-rank P value.

## Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "After induction therapy, patients who achieved complete response, were registered at the Hematology Division Office of the University of Naples and then assigned by using a computerized randomization system."
Allocation concealment (selection bias)	Low risk	Quote: "After induction therapy, patients who achieved complete response, were registered at the Hematology Division Office of the University of Naples and then assigned by using a computerized randomization system."
Blinding of participants and personnel (perfor- mance bias) Objective outcomes	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.
Blinding of outcome assessment (detection bias) Time-to-detection of recurrence	Unclear risk	Assessors were not blinded and as some of the clinical outcomes were based on judgements, the likely direction of bias cannot be predicted.
Incomplete outcome data (attrition bias) Objective outcomes	Low risk	No participant was lost to follow-up.



Picardi 2014 (Continued)				
Selective reporting (reporting bias)	Unclear risk	No protocol available, however outcomes mentioned in the aims were reported		
Other bias	Unclear risk	We detected no other bias.		

### Pietra 1998

Allocation concealment

(selection bias)

Methods	Randomised trial		
	More intensive clinical examinations and procedures vs standard follow-up		
	Cancer site: colorectal cancer		
	Setting: hospital, Italy		
	Accrual: 1987-1990		
	Duration of follow-up: 5 years		
Participants	207 patients who had undergone curative resections for primary untreated colorectal carcinoma.		
	Age (median/SD): intensive group: 62.2 (11) years; standard group: 64.4 (12) years		
	Sex: intensive group: male 56%, female 44%; standard group: male 51%, female 49%		
Interventions	Intervention group: intensive group, n = 104		
	"The patients were checked every three months during the first two years, at six-month intervals for three years, and once a year thereafter. Clinical examination, ultrasound, and CEA measurement were performed at each visit, and chest x-ray, colonoscopy, and CT were performed once a year."		
	• Comparison group: standard follow-up, n = 103		
	"The patients were seen at six-month intervals for one year, and once a year thereafter. Clinical examination, ultrasound, and carcinoembryonic antigen (CEA) measurement were performed at each visit, and chest x-ray and colonoscopy were performed once a year."		
Outcomes	Survival, detection of local recurrence		
Funding	None reported		
Notes	This study did not provide the required data for inclusion in the meta-analyses.		
	We contacted study authors in July 2018 for information on an exact log-rank test P value. No reply to date		
Risk of bias			
Bias	Authors' judgement	Support for judgement	
Random sequence generation (selection bias)	Unclear risk	Quote: "After surgery, patients were randomly assigned to have our existing conventional follow-up (Group A; n = 103) or intense follow-up (Group B; n = 104)."	
		Comment: sequence generation not reported	

Allocation concealment was not reported.

Unclear risk



Pietra 1998 (Continued)		
Blinding of participants and personnel (perfor- mance bias) Objective outcomes	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.
Blinding of outcome assessment (detection bias) Overall survival	Low risk	The outcome of survival is not likely to be biased.
Blinding of outcome assessment (detection bias) Time-to-detection of recurrence	Unclear risk	Assessors were not blinded and some of the clinical outcomes were based on judgements, but the likely direction of bias cannot be predicted.
Incomplete outcome data (attrition bias) Objective outcomes	Low risk	Quote: "All the patients were followed up prospectively, and the outcome was known for all of them at five years."
Selective reporting (reporting bias)	Unclear risk	No protocol available, however all outcomes mentioned in the aims were reported
Other bias	Unclear risk	We detected no other bias.

### Primrose 2014

Methods	Randomised trial, 4 arms		
	More intensive (CEA, CT or CEA+CT) vs minimal follow-up		
	Cancer site: colorectal cancer  Setting: 39 NHS hospitals in the UK		
	Accrual: January 2003-August 2009		
	Duration of follow-up: mean follow-up of 4.4 years (SD 0.8)		
Participants	1211 patients who had undergone curative treatment for primary colorectal cancer with no residual disease, microscopically clear margins, and Dukes stage A-C (TNM stage 1-3)		
	Age (mean): 69 years		
	Sex: male 61.2%, female 38.8%		
Interventions	• Intervention group 1: CEA group, n = 302		
	"Measurement of blood CEA every 3 months for 2 years, then every 6 months for 3 years, with a single chest, abdomen, and pelvis CT scan at 12 to 18 months if requested at study entry by hospital clinician."		
	<ul> <li>Intervention group 2: CT follow-up, n = 302</li> </ul>		
	"CT of the chest, abdomen, and pelvis every 6 months for 2 years, then annually for 3 years."		
	<ul> <li>Intervention group 3: CEA+CT follow-up, n = 303</li> </ul>		
	"Both blood CEA measurement and CT imaging as above."		
	• Comparison group: minimal follow-up, n = 304		



Primrose 2014 (Continued)	"No scheduled follow-up except a single CT scan of the chest, abdomen, and pelvis at 12 to 18months if requested at study entry by the hospital clinician."	
Outcomes	Primary outcome: surgical treatment of recurrence with curative intent after a minimum of 3 years of follow-up	
	Secondary outcomes: mortality (total deaths and deaths due to colorectal cancer), time to detection of recurrence, and survival after treatment of recurrence with curative intent	
Funding	The project was funded by the UK NIHR Health Technology Assessment (NIHR HTA) programme (project No. 99/10/99).	
Notes	We contacted study authors to request information on log-rank test P value for survival curves combining the research arms vs control arm. No reply to date	
	Possible conflicts of interest: GP Update Ltd	
Risk of hias		

#### Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Randomization to 1 of 4 groups (Figure 1) on a 1:1:1:1 ratio was performed centrally at the Oxford Clinical Trials Unit using a minimization algorithm to balance patient characteristics within each center based on 3 variables: adjuvant chemotherapy, sex, and age group."
Allocation concealment (selection bias)	Low risk	Quote: "Study nurses contacted the Oxford Clinical Trials Unit by telephone to enter a patient in the trial, reporting the relevant patient characteristics; they were then told the trial group to which the patient had been allocated."
Blinding of participants and personnel (perfor- mance bias) Objective outcomes	Unclear risk	Quote: "Because this was a pragmatic open trial, it was not possible to conceal the allocation group from either participants or clinicians."
Blinding of outcome assessment (detection bias) Overall survival	Low risk	The outcome of survival is not likely to be biased.
Blinding of outcome assessment (detection bias) Time-to-detection of recurrence	Unclear risk	Assessors were not blinded and some of the clinical outcomes were based on judgements, but the likely direction of bias cannot be predicted.
Incomplete outcome data (attrition bias) Objective outcomes	Low risk	Attrition seemed to be similar in all groups.
Selective reporting (reporting bias)	Unclear risk	No protocol available however the outcomes mentioned in the aims were reported
Other bias	Unclear risk	We detected no other bias.

## Rodríguez-Moranta 2006

Methods Randomised trial



Rodríguez-Moranta 2006 (Col			
	_	ostic procedures vs simple follow-up	
	Cancer site: colorectal		
	Setting: Hospital Clinic de Vic, Vic, Spain	of Barcelona, Barcelona; Hospital de Terrassa, Terrassa; and Hospital General	
	Accrual: January 1997-	December 2001	
		the median follow-up was 49 months (range, 24-87 months) in the intensive months (range, 21-86 months) in the simple strategy group.	
Participants	270 patients undergoir	ng curative resection for newly diagnosed colorectal cancer (TNM stage II/III)	
	Age (mean/SD): intensive: 67 (12) years; simple: 69 years (11) years		
	Sex: intensive: 61% ma	ıle; 39% female; simple: 63% male, 37% female	
Interventions	Intervention group:	intensive strategy, n = 133	
	"Patients in both simple and intensive surveillance groups underwent regular clinical review, including history, physical examination, and laboratory analyses (CBC, liver function tests, and serum CEA concentration) every 3 months for the first 2 years and every 6 months for years 3, 4 & 5.		
	Patients in the intensive strategy also underwent abdominopelvic CT (in those patients in whom primary tumor was located at rectum) or abdominal ultrasonography (in those patients in whom primary tumor was located at colon) every 6 months for the first 2 years and annually for years 3, 4 & 5. Chest radiograph and colonoscopy were carried out annually for 5 years."  • Comparison group: simple strategy, n = 137		
	"Patients underwent radiologic and endoscopic procedures only when tumor relapse was suspected according to any clinical or blood test abnormality. However, patients with hereditary nonpolyposis colorectal cancer or synchronous colorectal neoplasm who were allocated to the simple strategy underwent colonoscopy at 1 and 3 years of follow-up because of their high risk for metachronous lesions."		
Outcomes	Overall mortality, tumor recurrence amenable to curative-intent surgery, efficacy of each individual surveillance method overall and in every follow-up period, and costs		
Funding	Supported by grants from the Agència d'Avaluació de Tecnologia Mèdica of the Generalitat de Catalunya (2/6/96), from the Instituto de Salud Carlos III (Grants No. RC03/02 and RC03/10), and from the Ministerio de Ciencia y Tecnología (Grant No. SAF 04-07190). F.RM. received a research grant from the Hospital Clínic and the Instituto de Salud Carlos III, and V.P. received a grant from the Institut d'Investigacions Biomèdiques August Pi i Sunyer.		
Notes	We contacted study authors in July 2018 for confirmation that the P value reported was from a log-rank test. Study authors replied confirming that it was.		
Risk of bias			
Bias	Authors' judgement	Support for judgement	
Random sequence generation (selection bias)	Low risk	Quote: "Patients were randomly allocated to either simple or intensive surveil- lance strategies by means of sealed envelopes containing computer-generat- ed random numbers."	
Allocation concealment (selection bias)	Low risk	Quote: "Patients were randomly allocated to either simple or intensive surveil- lance strategies by means of sealed envelopes containing computer-generat-	

ed random numbers."



Rodríguez-Moranta 2006 (Continued)		
Blinding of participants and personnel (perfor- mance bias) Objective outcomes	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.
Blinding of outcome assessment (detection bias) Overall survival	Low risk	The outcome of survival is not likely to be biased.
Blinding of outcome assessment (detection bias) Time-to-detection of recurrence	Unclear risk	Assessors were not blinded and some of the clinical outcomes were based on judgements, but the likely direction of bias cannot be predicted.
Incomplete outcome data (attrition bias) Objective outcomes	Low risk	No participant was lost during follow-up.
Selective reporting (reporting bias)	Unclear risk	No protocol available, however all the outcomes mentioned in the aims were reported
Other bias	Unclear risk	We detected no other bias.

### **ROGY 2015**

Methods	Randomised trial, pragmatic cluster design
	SCP vs usual care only
	Cancer site: endometrial and ovarian cancer
	Setting: 12 hospitals in the south of the Netherlands (6 hospitals randomised to each arm)
	Accrual: endometrial cancer (April 2011 and October 2012) or ovarian cancer (April 2011 and March 2014)
	Duration of follow-up: 24 months
Participants	395 women newly diagnosed for endometrial cancer (n = 296) or ovarian cancer (n = 174)
	Age (mean/SD) endometrial: SCP: 67.4 (9.1) years; comparison: 67.8 (8.9) years
	Age (mean/SD) ovarian: SCP: 63.6 (11.2) years; comparison: 64.3 (10.7) years
Interventions	• Intervention group: SCP, endometrial (n = 154) and ovarian (n = 61)
	"In the SCP care arm, oncology providers were instructed to provide an SCP to patients after surgery; to provide an updated SCP during follow-up visits if there were changes in the cancer, treatment, or specialists; and to send a copy of the SCP to the patient's primary care physician. Oncology providers attended an instruction evening and received practical guidelines on how to discuss the information in the SCP with their patients, and agreed about the minimal items that should be discussed with respect to diagnosis, treatment, and possible adverse effects. Because of the pragmatic approach, oncology providers in the SCP care hospitals were free to choose whether the gynecologist/gynecologic oncologist and/or oncology nurse provided the SCP, fitting their clinical practice."
	• Comparison group: usual care, endometrial (n = 142) and ovarian (n = 113)
	"In the usual care arm, oncology providers (i.e., gynecologists/gynecologic oncologists and oncology nurses) gave standard care according to the Dutch follow-up guidelines, recommending verbal and



ROGY 2015 (Continued)	written information about the period after treatment and follow-up, signs of recurrence, and hospital contact details."
Outcomes	Primary outcomes: participants' satisfaction with information provision and care
	Secondary outcomes: included participants' illness perceptions and health care use, HRQoL, anxiety and depression
Funding	Grant No. UVT-2010-4743 from the Dutch Cancer Society
	Cancer Research Award from the Dutch Cancer Society (Grant No. UVT-2009- 4349)
Notes	We contacted study authors in September 2017 for information on final scores for HRQoL, anxiety and depression. Study authors replied providing means and SDs from multilevel linear regression analysis that accounted for the cluster design. We report on the 2 cancer populations separately as the data were analysed separately and reported in separate publications.
	Possible conflicts of interest: Janssen Pharmaceuticals

### Risk of bias

Bias	Authors' judgement	Support for judgement	
Random sequence generation (selection bias)	Low risk	Quote: "Randomization to either usual care or SCP care at hospital level was performed with a table of random numbers"	
Allocation concealment (selection bias)	Low risk	Quote: "Performed with a table of random numbers by a researcher not involved in the study and blind to the identity of the hospitals."	
Blinding of participants and personnel (perfor- mance bias) Patient-reported out- comes	Low risk	Quote: "Because the health care providers administering the intervention have to know whether they have to provide either usual care or SCP care, it was not possible for them to be blinded to the group assignment. The participants on the other hand are unaware of the group assignment, as they are under the assumption that the hospital is providing usual care."  The study is single-blinded as participants were blinded and because of the cluster-randomisation design, performance bias is unlikely.	
Blinding of outcome assessment (detection bias) Patient-reported outcomes	Low risk	Participants were self-assessors and were blinded to whether they receive care as usual or SCP.	
Incomplete outcome data (attrition bias) Patient-reported out- comes	High risk	At 12 months' follow-up, half of the participants did not return questionnaires	
Selective reporting (reporting bias)	Low risk	The reported outcomes were in accordance with the study protocol.	
Other bias	Unclear risk	We detected no other bias.	

### Rosselli Del Turco 1994

Methods	Randomised trial
	More intensive diagnostic tests vs clinical follow-up



Rosselli De	l Turco 1994	(Continued)
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Cancer site: breast cancer

Setting: 12 breast cancer clinics in different areas in Italy

Accrual: January 1985-December 1986

Duration of follow-up: 5 years ending December 1991

#### **Participants**

1243 premenopausal and post-menopausal patients surgically treated for histologically confirmed unilateral invasive breast carcinoma with no evidence of metastases

Age (mean/SD): not reported

#### Interventions

• Intervention group: intensive follow-up, n = 622

"Physical examination was performed every 3 months in the first 2 years and every 6 months in the following 3 years; two-view chest roentgenography and bone scan were performed every 6 months and mammography was performed every year until the end of the study (5 years)."

• Comparison group: clinical follow-up, n = 621

"Physical examination was performed every 3 months in the first 2 years and every 6 months in the following 3 years; mammography was performed every year during the study (5 years). Other diagnostic tests were performed only in the presence of symptoms suggestive of cancer recurrence."

#### Outcomes

Relapse-free survival and overall survival

#### **Funding**

National Research Council Applied Project Oncologica grant 84.00773.44

#### Notes

Bias	Authors' judgement Support for judgement	
Random sequence generation (selection bias)	Low risk	Quote: "Randomization was centrally performed by the coordinating center in Florence and stratified in blocks by center only"
Allocation concealment (selection bias)	Low risk	Quote: "Individual case allocation was communicated by telephone to the participating centers after enrolment"
Blinding of participants and personnel (perfor- mance bias) Objective outcomes	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.
Blinding of outcome assessment (detection bias) Overall survival	Low risk	The outcome of survival is not likely to be biased.
Blinding of outcome assessment (detection bias) Time-to-detection of recurrence	Unclear risk	Assessors were not blinded and some of the clinical outcomes were based on judgements, but the likely direction of bias cannot be predicted.
Incomplete outcome data (attrition bias) Objective outcomes	Unclear risk	161 participants were lost to follow-up (86 vs 75), reasons were not reported.



Rosselli Del Turco 1994 (Continued)			
Selective reporting (reporting to large the porting bias)  No protocol available, however all the outcomes mentioned in the porting bias.		No protocol available, however all the outcomes mentioned in the aims were reported.	
Other bias	Unclear risk	We detected no other bias.	

## **Ruddy 2016**

Methods	Randomised trial		
	Co-ordinated care with SCP vs standard follow-up only		
	Cancer site: breast cancer		
	Setting: the Dana-Farber Breast Oncology Clinic, USA		
	Accrual: January 2011-April 2013		
	Duration of follow-up: 12 months		
Participants	100 English-speaking women who were ≥ 18 years old and had pathologically confirmed stage 0-IIIa breast cancer		
	Age (median/IQR): intervention group: 57 (50-64) years; standard care group; 52 (45-63) years		
Interventions	Intervention group: co-ordinated care group (CC) including SCP and nurse-navigator, n = 50		
	"Patients received an SCP between 0 and 45 days after the end-of-active-treatment date. The SCP included details about the patient's tumor characteristics, therapies received (including dates, systemic therapy regimens, total chemotherapy dosages, toxicities, surgeries, and radiation doses), full contact information for providers, the name of the coordinator of continuing care, screening recommendations, a recommendation for referral to genetic counseling if appropriate, and details about the recommended visit frequency for her oncology providers and PCPs, with an emphasis on trying to avoid seeing more than 1 of these physicians within 3 months of each other. A history and a physical examination were recommended every 3 to 6 months for the first year of follow-up for all patients. The navigator then called CC patients or attempted to meet with them in person every 3 months throughout the next year (at least at 3, 6, and 9 months with an optional contact at 12 months) to try to coordinate their care."		
	• Comparison group: standard care, n = 50		
	"Those randomized to SC then received standard follow-up care and did not receive an SCP or contact from a patient navigator. This standard follow-up care was at the discretion of each SC patient's providers and was not dictated by the study."		
Outcomes	The proportion of participants who had at least 2 breast or chest wall examinations within 30 days of each other without a new related complaint (redundant care), anxiety and depression (GHQ-12), QoL (a modified version of the MOS-SF-12), and satisfaction with care (PSQ-18)		
Funding	This study was funded by institutional funds at the Dana-Farber Cancer Institute. Kathryn J. Ruddy's effort was partially supported by KL2TR000136-09 from the National Center for Advancing Translational Sciences, a component of the National Institutes of Health.		
Notes	This study did not provide the required data for inclusion in the meta-analyses.		
	Possible conflicts of interest: Neon Therapeutics		
Risk of bias			



### Ruddy 2016 (Continued)

Bias	Authors' judgement Support for judgement		
Random sequence generation (selection bias)	Unclear risk	Quote: "Female patients with early-stage breast cancer were randomized 1:1 to either standard care (SC) or coordinated follow-up care."	
		Comment: Sequence generation is not reported	
Allocation concealment (selection bias)	Unclear risk	Allocation concealment not reported	
Blinding of participants and personnel (perfor- mance bias) Objective outcomes	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.	
Blinding of participants and personnel (perfor- mance bias) Patient-reported out- comes	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.	
Blinding of outcome assessment (detection bias) Patient-reported outcomes	Unclear risk	Participants were self-assessors and were not blinded but the likely direction of bias cannot be predicted.	
Incomplete outcome data (attrition bias) Objective outcomes	Low risk	Numbers and reasons for attrition seem to be similar in both arms	
Incomplete outcome data (attrition bias) Patient-reported out- comes	Low risk	Numbers and reasons for attrition seem to be similar in both arms	
Selective reporting (reporting bias)	High risk	No protocol available. Results for anxiety and depression were not reported, even though it was an outcome mentioned in the methods.	
Other bias	High risk	Quote: "Although our navigator-led coordinated care intervention for breast cancer survivors was not effective in reducing the proportion of patients who had redundant breast examinations, these null results were likely biased by an unanticipated overrepresentation of patients receiving trastuzumab in the CC arm. Because trastuzumab is given every 3 weeks over a year and because patients are usually seen by an oncology provider every 9 weeks during this time, this uneven distribution of trastuzumab recipients likely added substantially to redundant care in the CC arm."	

### Rustin 2007

Methods

Randomised trial

Less intensive (2 CT scans) vs more intensive (5 CT scans) follow-up

Cancer site: testicular cancer

Setting: 32 cancer centres in the UK, Norway, Australia, and New Zealand



Rustin 2007 (Continued)			
(commutes)	Accrual: February 1998 and April 2003  Duration of follow-up: up to 84 months (median of 40 months)		
Participants	414 patients with stage I non-seminomatous germ cell tumours		
	Age (mean/SD): 2-scan arm: 31.6 (9.9) years 5-scan arm: 32.4 (10.1) years		
Interventions	Intervention and comparison arms not specified. We assume that the intervention was the less intensive arm.		
	<ul> <li>Intervention group: 2-scan arm, n = 247</li> </ul>		
	• Comparison group: 5-scan arm, n = 167		
	"Patients were randomized to surveillance with two CT scans over 1 year (at 3 and 12 months after orchidectomy) or five CT scans over 2 years (at 3, 6, 9, 12, and 24 months after orchidectomy)."		
Outcomes	The primary outcome was the proportion of all randomly assigned participants relapsing with intermediate- or poor-prognosis disease. Secondary outcomes were Royal Marsden Hospital stage at relapse, size of abdominal mass at relapse, time to detection of relapse, and first investigation to suggest relapse.		
Funding	Not reported		
Notes			

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Treatment was allocated using minimization and was stratified according to center and presence of vascular invasion."
Allocation concealment (selection bias)	Low risk	Quote: "Random assignment was performed by telephoning the MRC CTU."
Blinding of participants and personnel (perfor- mance bias) Objective outcomes	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.
Blinding of outcome assessment (detection bias) Time-to-detection of recurrence	Unclear risk	Assessors were not blinded and as some of the clinical outcomes were based on judgements, the likely direction of bias cannot be predicted.
Incomplete outcome data (attrition bias) Objective outcomes	Low risk	All participants were followed up and similar adherence to protocol for both groups
Selective reporting (reporting bias)	Low risk	All outcomes mentioned in the clinical trials registry were reported.
Other bias	Unclear risk	We detected no other bias.



Sc	hoema	ker 1998
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Methods	Randomised trial		
	More intensive diagnostic tests vs standard follow-up		
	Cancer site: colorectal cancer		
	Setting: university hospital in South Australia		
	Accrual: June 1984 and December 1990		
	Duration of follow-up: minimum of 5 years or until their death		
Participants	325 patients undergoing curative resection for newly diagnosed colorectal cancer		
	Age (mean/range): standard group: 69 (29-83 )years		
	Intensive group: 67 (30-84 )years		
	Sex: standard group: 98 men and 60 women; intensive group: 109 men and 58 women		
Interventions	<ul> <li>Intervention group: intensive, n = 167</li> <li>Comparison group: standard, n = 158</li> </ul>		
	"Patients in both standard and intensive follow-up groups underwent regular clinical review including history, examination, and screening investigations: three monthly for 2 years, and thereafter, six monthly for 5 years. Screening investigations at each follow-up consisted of complete blood profile, live function test, carcinoembryonic antigen (CEA), and fecal occult blood testing using the Haemoccult 2 test (without rehydration) on three fecal samples. Patients in the intensive arm of the trial in addition underwent yearly CXR, CT of the liver, and colonoscopy. Patients in the standard group to undergo CXR, CT of the liver, and colonoscopy only if indicated."		
Outcomes	5-year survival rate		
Funding	Supported by grants from the Anti-Cancer Foundation of the Universities of South Australia and the Commonwealth Health and Medical Research Council of the Department of Veteran's Affairs.		
Notes			

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The cards had been previously randomized using random tables."
Allocation concealment (selection bias)	High risk	Quote: "The patients were then randomized to either standard or intensive follow-up by choosing the next card from a box of cards indicating the type of follow-up."
		Comment: cards do not appear to be concealed.
Blinding of participants and personnel (perfor- mance bias) Objective outcomes	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.
Blinding of outcome assessment (detection bias) Overall survival	Low risk	The outcome of survival is not likely to be biased.



Schoemaker 1998 (Continued)		
Incomplete outcome data (attrition bias) Objective outcomes	Low risk	Similar numbers lost in both groups for similar reasons.
Selective reporting (reporting bias)	Unclear risk	No protocol available, however the outcome specified was reported.
Other bias	Unclear risk	We detected no other bias.

#### **Secco 2002**

Methods	Randomised trial, multi-armed			
	More intensive (risk adapted, high or low) vs minimal follow-up			
	Cancer site: colorectal cancer			
	Setting: hospital in Italy			
	Accrual: January 1988 and December 1996			
	Duration of follow-up: 5 years			
Participants	337 patients with primary colorectal cancer with no distant metastases and treated by curative surgery alone			
	Age (median/range)			
	Group 1 high-risk adapted: 67 years (32-86)			
	Group 1 low-risk adapted: 64 years (38-84)			
	Group 2 high-risk minimal: 63 years (29-85)			
	Group 2 low-risk minimal: 66 years (30-87)			
	Sex			
	Group 1 high-risk adapted: male 49%, female 51%			
	Group 1 low-risk adapted: male 50%, female 50%			
	Group 2 high-risk minimal: male 44% female 56%			
	Group 2 low-risk minimal: male 51%, female 49%			

#### Interventions

### Comparison 1

• Intervention group: high-risk participants in risk-adapted follow-up, n = 108

"Patients at high risk underwent intensive follow-up surveillance: clinical visits and serum CEA tests were performed every 3 months over the first 24 months, every 4 months in the third year and every 6 months in the fourth and fifth years. Abdominal and pelvic US was performed every 6 months over the first 36 months and every year at the fourth and fifth years. Rigid rectosigmoidoscopy for patients with rectal cancer and chest X-ray were performed once a year for 5 years."

• Comparison group: high-risk participants in minimal follow-up, n = 84

"Every 6 months they were expected to talk to the surgical team by telephone. The operated patients underwent clinical controls administered by their physician once a year or at any time on request and by telephone follow-up."



Secco 2002 (Continued)

#### **Comparison 2**

• Intervention group: low-risk participants in risk-adapted follow-up, n = 84

"Patients at low risk of recurrence underwent low intensity follow-up: clinical visits and serum CEA every 6 months over the first 24 months and once a year at the third, fourth and fifth years; abdominal and pelvic ultrasound (US) every 6 months in the first two years and once a year afterwards. Rigid rectosigmoidoscopy for patients with rectal cancer was performed once a year during the first two years and every 2 years afterwards, chest X-ray once a year over the whole follow-up period."

• Comparison group: low-risk participants in minimal follow-up, n = 61

"Every 6 months they were expected to talk to the surgical team by telephone. The operated patients underwent clinical controls administered by their physician once a year or at any time on request and by telephone follow-up."

#### Outcomes

- The efficacy of follow-up as defined by the number of asymptomatic recurrences detected during periodic visits or programmed diagnostic tests and who survived after surgical treatment for recurrence, divided by the number of all participants included.
- 2. The annual and total costs (EUR) of risk-adapted follow-up over a period of 5 years were calculated as recurrence if they were in the following categories: the sums of the cost of each diagnostic test considering the costs of materials, of depreciation of equipment and cost of medical personnel, technicians and nursing staff per minute.
- 3. 5-year survival in the different groups.

# Funding Not reported

#### Notes

This study did not provide the required data for inclusion in the meta-analyses.

We contacted study authors in July 2018 for information regarding log-rank P values for each research arm vs control arm. Study authors replied that they were unable to provide additional information.

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients of each group were randomly included in a long-term survival of the following variables: prognostic risk-adapted follow-up (group 1) or minimal follow-up factors, curative re-operation and type of follow-up programme performed by physicians (group 2)."
		Comment: the sequence generation was not reported.
Allocation concealment (selection bias)	Unclear risk	Allocation concealment was not reported.
Blinding of participants and personnel (perfor- mance bias) Objective outcomes	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.
Blinding of outcome assessment (detection bias) Overall survival	Low risk	The outcome of survival is not likely to be biased.
Blinding of outcome assessment (detection bias) Time-to-detection of recurrence	Unclear risk	Assessors were not blinded and some of the clinical outcomes were based on judgements, but the likely direction of bias cannot be predicted.



Secco 2002 (Continued)		
Incomplete outcome data (attrition bias) Objective outcomes	Unclear risk	Quote: "Twenty-one (5.8%) patients dropped out over the first 13 months: eight cases from group I and 13 from group 2."
objective outcomes		Comment: reasons for dropouts were not reported.
Selective reporting (reporting bias)	Unclear risk	No protocol available, however the outcomes mentioned in the aims were reported.
Other bias	Unclear risk	Baseline characteristics were not described in the text but data were presented in a table and there appeared to be baseline differences with regard to CEA levels. However, the direction of bias is difficult to predict.

### **Sheppard 2009**

Methods	Randomised trial		
	Patient-initiated vs specialist follow-up		
	Cancer site: breast cancer		
	Setting: a specialist breast unit in Portsmouth, UK		
	Accrual: September 2003-April 2005		
	Duration of follow-up: 18 months		
Participants	237 women diagnosed 2 years prior, who were not undergoing current treatment (except endocrine therapy)		
	Age (mean/SD): intervention group 57 (11) years; control group 58 (10.7) years		
Interventions	Intervention group: point-of-need access, n = 107		
	"Patients randomised to point of need access were given information of how to contact the breast care nurse if concerned (prior to commencement of the study two breast care nurses underwent training in clinical examination, physical assessment and subsequent management of symptoms (Table 1). The specialist team and the GP were informed and any outstanding routine appointments were cancelled, but mammograms continued on an annual basis."		
	<ul> <li>Comparison group: routine clinical follow-up, n = 107</li> </ul>		
	"Patients randomised to 6-monthly reviews received further follow up appointments for clinical review recurring every 6 months with an annual mammogram."		
Outcomes	Primary outcomes: psychological morbidity (GHQ-12) and QoL measured (FACT-B/ES).		
	Secondary outcomes: assessment of fear, isolation and the recording of "clinical events". Fear of recurrence was measured using a 3-item questionnaire designed by the author of FACT-G.		
Funding	Wessex Cancer Trust		
Notes	This study did not provide the required data for inclusion in the meta-analyses. Study authors did not report the number of participants randomised to each group, only the number of participants who completed the study in each arm.		
Risk of bias			
Bias	Authors' judgement Support for judgement		



Sheppard 2009 (Continued)		
Random sequence generation (selection bias)	Low risk	Quote: "Patients were randomised by the research nurse using a sequential series of sealed envelopes containing computer generated random assignments produced externally."
Allocation concealment (selection bias)	Low risk	Quote: "Prior to randomisation both the participants and the research nurse were blinded to group assignment."
Blinding of participants and personnel (perfor- mance bias) Objective outcomes	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.
Blinding of participants and personnel (perfor- mance bias) Patient-reported out- comes	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.
Blinding of outcome assessment (detection bias) Time-to-detection of recurrence	Unclear risk	Assessors were not blinded and as some of the clinical outcomes were based on judgements, the likely direction of bias cannot be predicted.
Blinding of outcome assessment (detection bias) Patient-reported outcomes	Unclear risk	Participants were self-assessors and were not blinded but the likely direction of bias cannot be predicted.
Incomplete outcome data (attrition bias) Objective outcomes	Unclear risk	Quote: "By November 2006, 214 patients had completed the study and this data is used for analysis; 23 patients were unable to complete the final questionnaire with 9 recurrences, 8 lost to follow up and 6 patients refusing to complete all of the data (Fig. 3)."
		Comment: attrition was not described in further detail.
Incomplete outcome data (attrition bias) Patient-reported out- comes	Unclear risk	Quote: "By November 2006, 214 patients had completed the study and this data is used for analysis; 23 patients were unable to complete the final questionnaire with 9 recurrences, 8 lost to follow up and 6 patients refusing to complete all of the data (Fig. 3)."
		Comment: attrition was not described in further detail.
Selective reporting (reporting bias)	Unclear risk	No protocol available, however the outcomes mentioned in the aims were reported.
Other bias	Unclear risk	We detected no other bias.

## Sobhani 2008

Methods	Randomised trial	
	More intensive (18FDG-PET) vs conventional follow-up	
	Cancer site: colorectal cancer	
	Setting: 7 teaching hospitals, France	
	Accrual: January 2001-June 2004	



Sobhani 2008 (Continued)	Duration of full account 24 months		
	Duration of follow-up: 24 months		
Participants	130 patients who had undergone curative treatment for colon or rectal cancer with absence of disease progression		
	Age (mean/SD): PET: 58.1 (11.2) years; conventional: 62 (12.1) years		
	Sex: not reported		
Interventions	<ul> <li>Intervention group: PET group, n = 65</li> <li>Comparison group: conventional group, n = 65</li> <li>"Comprised six visits, a physical examination, biomarker assays (serum CEA or CA19-9, or both), an ultrasound scan (US) every 3 months (except after 9 and 15 months of follow-up), a chest X-ray every 6 months, and abdominal CT scans after 9 and 15 months of follow-up.</li> <li>Patients in the PET group also underwent 18FDG-PET after 9 and 15 months."</li> </ul>		
Outcomes	The overall rate of recurrence in each group after 15-months' follow-up, the time to second-line surgical intervention and/or drug treatment, including either chemotherapy or palliative therapy and the overall rate of curative surgery, if any, in each study group		
Funding	PHRC and CEDIT (The French national funding scheme and the French Committee for Evaluation and Diffusion of Innovative Technologies)		
Notes			

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were randomly divided into two groups: One group received a conventional work-up (Con) and the other underwent PET."
		Comment: study did not report how the random sequence was generated
Allocation concealment (selection bias)	Unclear risk	Quote: "Patients were randomly divided into two groups: One group received a conventional work-up (Con) and the other underwent PET."
		Comment: study did not report if allocation was concealed
Blinding of participants and personnel (perfor- mance bias) Objective outcomes	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.
Blinding of outcome assessment (detection bias) Time-to-detection of recurrence	Unclear risk	Assessors were not blinded and as some of the clinical outcomes were based on judgements, the likely direction of bias cannot be predicted.
Incomplete outcome data (attrition bias) Objective outcomes	Low risk	Attrition was insignificant.
Selective reporting (reporting bias)	Unclear risk	No protocol available, however all outcomes mentioned in the aims were reported.
Other bias	Unclear risk	We detected no other bias.



### Sobhani 2018

Methods	Randomised trial	
	More intensive (18FD)	G-PET) vs conventional follow-up
	Cancer site: colorectal	cancer
	Setting: 12 gastro-intes	stinal oncology or surgery departments in university hospitals in France
	Accrual: 2008-2012	
	Duration of follow-up:	3 years
Participants	239 patients, aged ≥ 18 years with histologically proven colon or rectal adenocarcinoma and an Eastern Cooperative Oncology Group (ECOG) status of 0 or 1 were eligible if they were considered in remission and at high risk of recurrence after potentially curative surgery. High risk was defined as stage II colorectal cancer with tumour perforation or stage III or IV colorectal cancer with complete resection of all synchronous and metachronous metastases. To be eligible for the present study, patients had to be in remission 4-6 months after surgery	
	Age (median/IQR): inte	rvention: 63.4 (53.4-70.7) years; control: 61.6 (54.7-70.1) years
	Sex: intervention: 52.5	% men, 47.5% women; control: 58% men, 42% women
Interventions	• Intervention group:	
		conventional group, n = 119
	so underwent 18FDG-P examination and labor had 18FDG-PET/CT. Fol were performed in all p	tients underwent whole-body CT (wbCT) and those in the intervention arm al- ET/CT. In both groups, patients were evaluated every 3 months with a physical atory tests. Every 6 months, they had wbCT, and intervention-arm patients also low-up duration for the trial was 3 years. Liver ultrasound and chest radiography patients in both arms at the visits without wbCT (with or without 18FDG-PET/CT). If was performed routinely 1 and 3 years following primary CRC resection, as rec-
Outcomes	The primary end point was treatment failure defined as either unresectable recurrence or death from any cause.	
	The secondary end points were the mortality rate, incidence of recurrence, incidence of unresectable recurrence, times to resectable and unresectable recurrences, total number of recurrences, overall survival and disease-free survival.	
Funding	French Ministry of Health (grant PHRC 2007AOM07156 and PHRC 2009 AOM11324)	
Notes		
Risk of bias		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "A computer-generated random number sequence was prepared at the Henri Mondor University Hospital informatics department. Randomisation was stratified by centre and TNM stage (II/III/IV). Blocks of 4 were used."
Allocation concealment (selection bias)	Low risk	Quote: "The random numbers were placed in consecutively numbered, sealed, opaque envelopes. Study inclusion was performed by a clinical research assistant at each centre, who determined the random allocation group of each participant by selecting the envelope with the next available number."



Sobhani 2018 (Continued)		
Blinding of participants and personnel (perfor- mance bias) Objective outcomes	Unclear risk	Given the nature of this study blinding of participants and personnel was not possible
Blinding of outcome assessment (detection bias) Overall survival	Low risk	The outcome of survival is not likely to be biased.
Blinding of outcome assessment (detection bias) Time-to-detection of recurrence	Unclear risk	Assessors were not blinded and as some of the secondary objective outcomes were based on judgements, the likely direction of bias cannot be predicted.
Incomplete outcome data (attrition bias) Objective outcomes	Low risk	Only 1 participant was lost to follow-up.
Selective reporting (reporting bias)	Low risk	All the outcomes specified in the protocol were reported.
Other bias	Unclear risk	Quote: "Despite the two groups appeared well balanced at baseline, we cannot be entirely sure that consecutive patients were considered for enrolment in all centres."
		Comment: possibility of selection bias

### Van der Meulen 2013

Methods	Randomised trial	
	Addition of nurse-led psychosocial package (NUCAI) vs usual care only	
	Cancer site: head and neck cancer	
	Setting: hospital, the Netherlands	
	Accrual: January 2005-September 2007	
	Duration of follow-up: 1 year	
Participants	205 patients with diagnosis of squamous cell carcinoma of the oral cavity, oropharynx, hypopharynx, or larynx who had undergone treatment with curative intent	
	Age (mean/SD): NUCAI: 60.1 (9.8) years; usual care: 60.7 (9.8) years	
	Sex: NUCAI: 70.5% men, 29.5% women; usual care: 70.3% men, 29.7% women	
Interventions	Intervention group: NUCAI, n = 103	
	"The intervention was nurse-led and offered in combination with regular medical follow-up visits at the University Medical Center Utrecht, the Netherlands. (See description of usual care the comparison group). The NUCAI consists of six components: evaluating current mental status with the Hospital Anxiety and Depression Scale (HADS); discussing current problems; systematically asking about physical problems and functioning in six relevant life domains; providing the Adjustment to Fear, Threat or Expectation of Recurrence (AFTER) intervention, if indicated; providing general medical assistance and advice, if indicated; and referring patients to psychological aftercare, if indicated."	
	• Comparison group: usual care, n = 102	



V	an d	ler N	/leul	len	2013	(Continued)
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"Care as usual was provided by HNC specialists and was primarily aimed at the treatment of complications and the detection of recurrences or second primary tumors. Patients were seen at 2-month intervals for a 10-minute appointment, during which they were examined, their physical history was reviewed, and ancillary tests were ordered if necessary."

#### Outcomes

The primary end point was depressive symptoms (CES-D scale) and the secondary end point was physical symptoms at 12 months after completion of cancer treatment (the head and neck module of the EORTC-QLQ.

Funding

This research was funded by a grant from the Dutch Cancer Society.

Notes

This study did not provide the required data for inclusion in the meta analyses.

#### Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "After the completion of cancer treatment, the patients were randomized using an open block procedure to receive NUCAI or care as usual, stratified by gender and tumor stage."
Allocation concealment (selection bias)	Low risk	Quote: "After the completion of cancer treatment, the patients were randomized using an open block procedure to receive NUCAI or care as usual, stratified by gender and tumor stage."
Blinding of participants and personnel (perfor- mance bias) Patient-reported out- comes	Low risk	Participants were not aware if they received intervention or usual care. Due to the nature of this study is was not possible to double-blind.
Blinding of outcome assessment (detection bias) Patient-reported outcomes	Low risk	Participants were self-assessors and were blinded to allocation.
Incomplete outcome data (attrition bias) Patient-reported out- comes	Low risk	According to the CONSORT diagram approximately similar numbers of participants were lost to follow-up for the same reasons.
Selective reporting (reporting bias)	Unclear risk	No protocol available, however all outcomes mentioned in the aims were reported.
Other bias	Unclear risk	We detected no other bias.

### Verschuur 2009

Methods

### Randomised trial

### Nurse-led vs standard surgeon-led

Cancer site: oesophageal cancer

Setting: (Erasmus MC – University Medical Center Rotterdam and Reinier de Graaf Hospital, Netherlands



Verschuur 2009 (Continued)	Accrual January 2004	Fahruany 2006		
	Accrual: January 2004-	•		
	Duration of follow-up:	12 months		
Participants	109 patients 3 weeks after hospital discharge following intentionally curative surgery for oesophagor gastric cardia cancer			
	Age (mean/SD): nurse-	led: 61 (9) years; standard follow-up: 61 (7) years		
	Sex: male 74%, female	26%		
Interventions	Intervention group:	nurse-led, n = 54		
	perience in oncologica sophageal and gastric	vas performed by home visits of a specialist nurse with more than 10 years ex- l care. Didactic training included a syllabus on diagnosis and treatment of oe- cardia cancer, potential problems after oesophageal resection and medical-legal w-up visits for both follow-up groups were 6 weeks, and 3, 6, 9 and 12 months af-		
	• Comparison group: usual care, n = 102			
	"Standard follow-up was performed by a group of two senior surgeons at the outpatient clin Erasmus MC Rotterdam and one senior surgeon at the Reinier de Graaf Hospital Delft. Sched low-up visits for both follow-up groups were 6 weeks, and 3, 6, 9 and 12 months after randor			
Outcomes	Survival, health-related	d QoL (EORTC, EuroQol-5D), participant satisfaction and costs		
Funding	This study was supported by a grant from the Health Care Research Program Erasmus MC Rotterdam and the Dutch Digestive Disease Foundation (SWO 02-04).			
Notes	Survival data was reported in results but not methods. We contacted study authors regarding whether they used a log-rank test. No reply.			
Risk of bias				
Bias	Authors' judgement	Support for judgement		
Random sequence generation (selection bias)	Low risk	Quote: "Randomisation was performed centrally by the Trial Office of the Department of Oncology, Erasmus MC Rotterdam, using computer-generated lists."		
Allocation concealment (selection bias)	Low risk	Quote: "Randomisation was performed centrally by the Trial Office of the Department of Oncology, Erasmus MC Rotterdam, using computer-generated lists."		
Blinding of participants and personnel (perfor- mance bias) Objective outcomes	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.		
Blinding of participants and personnel (perfor- mance bias) Patient-reported out- comes	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.		
Blinding of outcome assessment (detection bias) Overall survival	Low risk	The outcome of survival is unlikely to be biased.		



Verschuur 2009 (Continued)		
Blinding of outcome assessment (detection bias) Patient-reported outcomes	Unclear risk	Participants were self-assessors and were not blinded but the likely direction of bias cannot be predicted.
Incomplete outcome data (attrition bias) Objective outcomes	Low risk	Only 2 participants were lost to follow-up and no participants were excluded from analyses.
Incomplete outcome data (attrition bias) Patient-reported out- comes	Low risk	Only 2 participants were lost to follow-up and no participants were excluded from analyses.
Selective reporting (reporting bias)	Unclear risk	No protocol available, however the outcomes mentioned in the aims were reported
Other bias	Unclear risk	We detected no other bias.

## **Wang 2009**

Methods	Randomised trial
	More intensive colonoscopy vs routine follow-up
	Cancer site: colorectal cancer
	Setting: teaching hospital in Sun Yat-Sen University, China
	Accrual: January 1994-March 2001
	Duration of follow-up: 5 years
Participants	326 patients undergoing radical surgery for colorectal cancer
	Age (mean/SD): intensive group: 54.6 (12.9) years; routine 54.4 (13.4) years
	Sex: intensive: 88 male and 77 female; routine: 89 male and 72 female
Interventions	<ul> <li>Intervention group: intensive colonoscopy, n = 165</li> <li>Comparison group: routine colonoscopy, n = 161</li> </ul>
	"All patients were expected to visit GI surgery as outpatients every 3 months for the first year, every 6 months for the next 2 years, and then annually for the next 2 years. During each visit, a medical history was obtained, a clinical examination was performed, CEA levels were determined, and chest x-ray and liver imaging (either CT or US) were performed. Patients in the ICS group underwent colonoscopy at each visit In the routine group colonoscopy was performed at 6, 30, and 60 months postoperatively (not necessary at 6 months if it had been performed preoperatively)."
Outcomes	The primary end point was overall survival. The secondary end point was postoperative colorectal cancer.
Funding	Not reported
Notes	
Risk of bias	



### Wang 2009 (Continued)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "The patients were then randomized to either the RCS group or the ICS group by means of sealed envelopes containing cards printed with ICS or RCS within each stratum."
		Comment: random sequence generation was not reported.
Allocation concealment (selection bias)	Low risk	Envelopes were sealed
Blinding of participants and personnel (perfor- mance bias) Objective outcomes	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.
Blinding of outcome assessment (detection bias) Overall survival	Low risk	The outcome of survival was unlikely to be biased.
Blinding of outcome assessment (detection bias) Time-to-detection of recurrence	Unclear risk	Assessors were not blinded and some of the clinical outcomes were based on judgements, but the likely direction of bias cannot be predicted.
Incomplete outcome data (attrition bias) Objective outcomes	Low risk	Similar numbers for loss to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol available, however the outcomes mentioned in the aims were reported.
Other bias	Unclear risk	We detected no other bias.

### Wattchow 2006

Methods	Randomised trial
	GP-led vs surgeon-led follow-up
	Cancer site: colon cancer
	Setting: hospital, Australia
	Accrual: March 1998-March 2001
	Duration of follow-up: 2 years
Participants	203 patients who had undergone surgery for colon cancer (including rectosigmoid) with histological grade Dukes stage A, B or C (cases of disseminated cancer were excluded).
	Age: reported as categories
	Sex: male: 117 (57.6%), female: 86 (42.4%)
Interventions	• Intervention group: GP-led, n = 97
	<ul> <li>Comparison group: surgeon-led, n = 106</li> </ul>



#### Wattchow 2006 (Continued)

"Follow-up guidance, based on current clinical practice and guidance was provided, and inserted into either the patient's GP or surgeon/hospital records. Nevertheless, in accordance with the study's pragmatic design there was no compulsion for clinicians in either setting to adhere to the guidance:

The patient should be reviewed 1. Three monthly for the first 2 years postoperatively 2. Then 6 monthly for the next 3 years Patient history Please ask the following (or similar) questions to your patient 1. What is your bowel habit? Has there been any change lately? 2. Have you noticed any bleeding in the stools or from the anus? 3. Have you experienced any abdominal pains of more than a few days' duration? 4. Have you experienced any other pains, for example in your back, chest or legs? 5. Have you noticed any weight loss? 6. Have you been feeling tired or lethargic? Physical examination Assess the patient for 1. Colour 2. Enlarged neck nodes 3. Abdominal masses, for example, the liver, wound deposits or ascites Diagnostic tests Recent studies have raised doubts as to the value of many diagnostic tests in the detection of recurrent or metastatic disease. However, there is value in performing. 1. Annual FOBT (faecal occult blood test) 2. A colonoscopy every 3 years."

#### Outcomes

Primary outcomes measured at baseline, 12 and 24 months

- QoL based on SF-12 PCS and MCS scores
- depression and anxiety (HADS)

measured at 24 months only:

· satisfaction (PSVQ)

Secondary outcomes measured at 24 months only:

- the number and type of investigations (blood tests, FOBT, colonoscopies and radiological investigations)
- number and time to detection of recurrences
- deaths from all causes at 2 years post-entry into the study

#### **Funding**

The trial was supported by grants from the National Health and Medical Research Council 1998-2001, Anti Cancer Foundation of South Australia 2002-2003.

Notes

We contacted study authors in July 2018 for information regarding number of recurrences in each arm to carry out calculations. No reply to date

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Consenting patients were then randomly allocated to either 'GP-led' or 'surgeon-led' follow-up using an Excel random number generator."
Allocation concealment (selection bias)	Low risk	Quote: "Randomisation was conducted by the study researchers, who were not involved in the design of the study or the clinical care of the patients, and was concealed until the interventions were assigned."
Blinding of participants and personnel (perfor- mance bias) Objective outcomes	Unclear risk	Given the nature of the study, it was not possible to blind participants and personnel.
Blinding of participants and personnel (perfor- mance bias) Patient-reported out- comes	Unclear risk	Given the nature of the study, it was not possible to blind participants and personnel.



Wattchow 2006 (Continued)		
Blinding of outcome assessment (detection bias) Overall survival	Low risk	The outcome of survival is not likely to be biased.
Blinding of outcome assessment (detection bias) Time-to-detection of recurrence	Unclear risk	Assessors were not blinded and as some of the clinical outcomes were based on judgements, the likely direction of bias cannot be predicted.
Blinding of outcome assessment (detection bias) Patient-reported outcomes	Unclear risk	Participants were self-assessors and were not blinded but the likely direction of bias cannot be predicted.
Incomplete outcome data (attrition bias) Objective outcomes	Low risk	Similar numbers and reasons for attrition in both groups.
Incomplete outcome data (attrition bias) Patient-reported out- comes	Low risk	Similar numbers and reasons for attrition in both groups.
Selective reporting (reporting bias)	Unclear risk	No protocol available, however the outcomes mentioned in the aims were reported
Other bias	Unclear risk	We detected no other bias.

### Westeel 2012

Methods	Randomised trial	
	More intensive (with CT-scans) vs minimal follow-up (only X-rays) (IFCT-0302 trial)	
	Cancer site: NSCLC	
	Setting: 7 hospitals in France	
	Accrual: January 2005-November 2012	
	Duration of follow-up: 5 years	
Participants	1775 patients with NSCLC after complete resection for a clinical stage I, II, IIIA and T4 (pulmonary nodules in the same lobe) N0-2	
Interventions	<ul> <li>Intervention group: intensive (CCT), n = 887</li> <li>Comparison group: minimal (CXR), n = 888</li> </ul>	
	"In the CXR arm, follow-up consisted of clinic visit and chest X-rays. In the CCT arm, patients underwent clinic visit, chest X-rays, thoraco-abdominal CT scan plus fiber optic bronchoscopy (only mandatory for squamous cell and large cell carcinomas). In both arms, procedures were repeated every 6 months after randomization during the first 2 years, and yearly until 5 years. Supplementary procedures were allowed in case of symptoms."	
Outcomes	Primary end point was overall survival	



Vesteel 2012 (Continued)		
Funding	PHRC National, Bourse de la Fondation Weisbrem-Benenson, Subvention des Laboratoires Lilly (France)	
Notes	Only conference abstracts available. We contacted study authors in June 2019 for additional data. Study authors replied with latest data on overall survival and disease-free survival. Risk of bias assessments carried out based on a translation of the protocol in French and from the conference abstracts	
Risk of bias		
Bias	Authors' judgement	Support for judgement
Random sequence genera- tion (selection bias)	Low risk	Quote: "By telephone call to a randomization center (ASCOPHARM)"
Allocation concealment (selection bias)	Low risk	Quote: "By telephone call to a randomization center (ASCOPHARM)"
Blinding of participants and personnel (perfor- mance bias) Objective outcomes	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.
Blinding of outcome as- sessment (detection bias) Overall survival	Low risk	The outcome of survival is unlikely to be biased.
Blinding of outcome as- sessment (detection bias) Time-to-detection of re- currence	Unclear risk	Assessors were not blinded and as some of the clinical outcomes were based on judgements, the likely direction of bias cannot be predicted.
Incomplete outcome data (attrition bias) Objective outcomes	Low risk	As data were obtained from hospital records, we judged that risk of attrition bias was low.
Selective reporting (re- porting bias)	Low risk	All outcomes specified in the clinicaltrials.gov entry were reported.
Other bias	Unclear risk	We detected no other bias.

## Wille-Jorgensen 2018

Methods	Randomised trial			
	More vs less frequent follow-up schedule			
	Cancer site: colorectal cancer stage II–III			
	Setting: 24 centres in Sweden, Denmark, and Uruguay			
	Accrual: January 2006-December 2010			
	Duration of follow-up: 5 years after surgery			
Participants	2555 patients who had undergone surgical resection with curative intent for colorectal adenocarcinoma (with or without adjuvant treatment), aged ≤ 75 years, provision of written informed consent			



#### Wille-Jorgensen 2018 (Continued)

for participation, a colon and rectum free of neoplasia verified by perioperative barium enema or a colonoscopy within 3 months after surgery, and tumour stage II or III (T3-T4, N0, M0, any N1-N2, M0)

Age (median/IQR): high-frequency follow-up: 65.2 (59.6-69.7) years; low-frequency follow-up 64.7 (58.6-69.9) years

Sex: high-frequency follow-up: 56.3% men, 43.7% women; low-frequency follow-up: 53.7% men, 46.3% women

#### Interventions

• Intervention group: high-frequency group, n = 1275

"Patients randomized to the high-frequency group were required to have follow-up testing with multislice contrast enhanced CT of the thorax and abdomen and CEA at 6, 12, 18, 24, and 36 months after surgery. Testing with a pelvic CT was not required."

• Comparison group: low-frequency group, n = 1280

"Patients randomized to the low-frequency group were required to have follow-up testing with multislice contrast-enhanced CT of the thorax and abdomen and CEA at 12 and 36 months after surgery. Testing with a pelvic CT was not required."

#### Outcomes

The primary outcomes were 5-year overall mortality and 5-year colorectal cancer–specific mortality rates. The secondary outcome was the colorectal cancer–specific recurrence rate during 5 years of follow-up.

#### **Funding**

This study was funded by unrestricted grants from the Nordic Cancer Union, A.P. Møller Foundation, Beckett Foundation, Grosserer Chr. Andersen og hustru bursary, Sigvald og Edith Rasmussens Memorial Fund, Martha Margrethe og Christian Hermansens Fund, the Danish Medical Association, the Danish Cancer Society, the Danish Council for Independent Research/Medical Sciences (all awarded to Dr Wille-Jørgensen), and by unrestricted grant CAN 2013/553 from the Swedish Cancer Foundation (awarded to Dr Påhlman).

Notes

Conflicts of interest: Dr Renehan reported receiving honoraria from Janssen-Cilag and Merck Serona for giving lectures

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Participating patients were randomized in block sizes of 10 by computer allocation to 1 of the 2 follow-up regimens."
Allocation concealment (selection bias)	Low risk	Quote: "The allocation procedure was concealed to the deliverers of treatment."
Blinding of participants and personnel (perfor- mance bias) Objective outcomes	Unclear risk	Given the nature of the study it was not possible to blind participants and physicians.
Blinding of outcome assessment (detection bias) Overall survival	Low risk	The outcome of survival is not likely to be biased.
Blinding of outcome assessment (detection bias) Time-to-detection of recurrence	Unclear risk	Assessors were not blinded and some of the clinical outcomes were based on judgements, but the likely direction of bias cannot be predicted.



Wille-Jorgensen 2018 (Continued)			
Incomplete outcome data (attrition bias) Objective outcomes	Low risk	Similar reasons and number of withdrawals and exclusions in each group	
Selective reporting (reporting bias)	Low risk	All the outcomes specified in the protocol were reported.	
Other bias	Unclear risk	Quote: "Turnover of responsible investigators and staff in many recruitment centres during a long study period is a possible weakness because any non-adherence to the protocol would most likely bias this trial's findings toward the null. Different and varying intensity of national follow-up regimes may have influenced the Low-intensity group. No national guidelines existed in Uruguay at the time of study initiation."	

### **Young 2013**

Methods	Randomised trial  Addition of the CONNECT intervention vs usual care only  Cancer site: colorectal cancer		
	Setting: hospital, Sydney, Australia		
	Accrual: July 2008-March 2011		
	Duration of follow-up: 6 months		
Participants	775 adult patients undergoing surgery for primary colorectal cancer		
	Age (Mean/SD): intervention group: 68.6 (2.2) years; comparison group: 67.0 (12.1) years		
	Sex: intervention group: 56.8% male; comparison group: 54.2% male		
Interventions	Intervention group: CONNECT, n = 398		
	"CONNECT is supplementary to usual follow-up care and involves no face-to-face contact. It consists of five scheduled, structured telephone calls on days 3 and 10 and then at 1, 3, and 6 months after hospital discharge. Each call includes 22 standardized screening questions about common physical, psychosocial, information, supportive care, and rehabilitation/follow-up needs. The intervention was delivered by experienced nurses who received training and ongoing debriefing by senior researchers with backgrounds in nursing, psychology, and medicine."		
	• Comparison group: usual care, n = 106		
	Usual care was not described.		
Outcomes	At 1, 3, and 6 months after discharge, participants were mailed questionnaires that included the FACT-C and Distress Thermometer tools and questions about postoperative health services' utilisation. The 3- and 6-month questionnaires also elicited participants' experience of cancer care co-ordination using a 20-item instrument, generating 1 total and 2 subscale (i.e. communication and navigation) scores, as well as the SupportiveCareNeeds Survey Short Form (SCNS-SF34), which measures unmet needs across 5 domains (psychological, health system and information, physical and daily living, participant care and support, and sexuality).		
Funding	Supported in part by Cancer Institute New South Wales Health Services Research Program Grant No. 06/HSG/1-08, which funds the CONNECT programme.		



#### Young 2013 (Continued)

Notes This study did not provide the required data for inclusion in the meta-analyses.

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Participants were stratified by hospital and randomly allocated to a study group using a computer-generated random-number list."
Allocation concealment (selection bias)	Low risk	Quote: "Patients were advised of their group allocation at day 3 after hospital discharge to ensure that this knowledge could not influence any clinical care or information provided by staff during admission."
Blinding of participants and personnel (perfor- mance bias) Patient-reported out- comes	Unclear risk	Given the nature of the study, it was not possible to blind participants or personnel.
Blinding of outcome assessment (detection bias) Patient-reported outcomes	Unclear risk	Participants were self-assessors and were not blinded but the likely direction of bias cannot be predicted.
Incomplete outcome data (attrition bias) Patient-reported out- comes	Low risk	Similar numbers of responses to questionnaires and participants lost to follow-up in the 2 groups.
Selective reporting (reporting bias)	Low risk	All outcomes registered in the Australian New Zealand Clinical Trials registry were reported except cost.
Other bias	Unclear risk	We detected no other bias.

Empty cells in the "Risk of bias" tables refer to instances where the specific risk of bias criterion did not apply, as this type of outcome was not reported by the study

18F-FDG-PET: 8F-fluoro-2-deoxy-D-glucose positron emission tomography; AJCC: American Joint Committee on Cancer; BSI-18: 18-item Brief Symptom Inventory; CaSUN: Cancer Survivors' Unmet Needs measure; CBC: complete blood count (blood test); CEA: carcinoembryonic antigen; CE-CT: contrast-enhanced computed tomography; CA19-9: cancer antigen 19-9; CES-D: Centre for Epidemiological Studies-Depression; CT: computed tomography; CWS: Cancer Worry Scale; CXR: chest X-ray; EORTC-QLQC-30: European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core; EPIC: Expanded Prostate Cancer Index Composite; EQ VAS: EQ visual analogue scale; FACT-G: Functional Assessment of Cancer Therapy - General; FACT-B/ES: Functional Assessment of Cancer Therapy - Breast and Endocrine subscales; FCIR: Fear of Cancer Recurrence Inventory; FDG-PET: fluorodeoxyglucose-positron emission tomography; FIGO: International Federation of Gynecology and Obstetrics; FOBT: faecal occult blood tests; GHQ-12: General Health Questionnaire-12; GP: general practitioner; HADS: Hospital Anxiety and Depression Scale; HL: Hodgkin lymphoma; HRQoL: health-related quality of life; HTA: Health Technology Assessment; IES: Impact of Event Scale; ITT: intention-to-treat; IQR: interquartile range; MCS: mental component summary; MOS-PSQ: Medical Outcomes Study-Patient Satisfaction Questionnaire; MOS-SF-12: Medical Outcomes Study Short Form 12; N/A: not applicable; NHS: National Health Service; NIHR: National Institute for Health Research; NSCLC: non-small cell lung cancer; PCAS: Primary Care Assessment Survey; PCS: physical component summary; PCP: primary care physician; PET-CT: positron emission tomography-computed tomography; PHQ: Patient Health Questionnaire; POMS: Profile of Mood States; PROMS: patient reported outcome measures; PSQ: Patient Satisfaction Questionnaire; PSVQ: Patient Visit-Specific Questionnaire; QLQ-INFO25: European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Cancer information; QLQ-OG25: European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Cancer of the oesophagus, oesophago-gastric junction and stomach; QOL: quality of life; SCP: survivorship care plan; SD: standard deviation; SF-12: Short Form Health Survey; SF-PSQ-18: 18item, short form patient satisfaction questionnaire; STAI: State Trait Anxiety Inventory; UCLA-PCI: University of California Los Angeles -Prostate Cancer Index; **US:** ultrasound



## **Characteristics of excluded studies** [ordered by study ID]

Study	Reason for exclusion	
Baildam 2002	Insufficient information, only conference abstract available. We contacted study author in September 2017, no reply to date	
Chang 2013	Wrong intervention	
Cruickshank 2015	Insufficient information, only conference abstract available. We contacted study author in September 2017, no reply to date	
Ebell 1998	Unable to locate journal or abstracts	
Faithfull 2001	Wrong outcomes	
Gulliford 1997	Wrong outcomes	
Haq 2015	Wrong outcomes	
Helgesen 2000	Wrong intervention. Watchful waiting/active surveillance	
Holtedahl 2005	Wrong patient population	
Jakobsen 2013	Insufficient information, only conference abstract available. Unable to locate any contact information for the study author	
Jefford 2011	Wrong outcomes	
Kessler 2013	Study never started due to lack of funding (information from e-mail reply from study author on 15 May 2019)	
Kew 2006	Unable to locate abstract	
Lanceley 2017	Wrong patient population. Includes patients "irrespective of remission."	
Lavau-Denes 2013	Insufficient information, only conference abstract available. Unable to contact study authors. Available e-mail addresses not valid	
Lyu 2016	Wrong outcomes	
Majhail 2019	Wrong intervention. Comparing use of SCPs in patients up to 5 years after treatment, not integrated as part of a new follow-up strategy	
Mathew 2014	Wrong intervention. Intervention of early vs delayed treatment	
Moore 2002	Wrong patient population	
NCT00049465	Wrong outcomes	
NCT01824745	Wrong outcomes	
NCT01973946	Wrong patient population	
NCT01993901	Study has been withdrawn	
NCT02200133	Wrong patient population. Includes patients who were not cured	



Study	Reason for exclusion		
NCT02209415	Wrong outcome: "Number of patients eligible for treatment."		
NCT02361099	Wrong patient population		
NCT02655068	Study has been withdrawn		
NCT03056469	Wrong patient population. Includes patients who were not curatively treated		
NCT03125070	Wrong intervention		
NCT03271099	Wrong outcomes		
NCT03360994	Wrong intervention. Same follow-up strategy in both groups but the intervention group receives their appointments online		
NCT03424837	Wrong patient population		
NCT03608410	Wrong patient population		
NCT03618017	Wrong outcomes		
Parker 2018	Wong outcomes		
Ploos van Amstel 2016	Wrong intervention		
Puri 2018	Wrong patient population. Includes those with recurrence		
Rogers 2018	Wrong design. A cluster-preference randomised trial where each arm contains consultants who receive their preferred arm and consultants who were randomised to the arm.		
Rustin 2010	Wrong intervention. Intervention of early vs delayed treatment		
Samawi 2017	Wrong design: not randomised		
Skolarus 2017	Wrong patient population. Includes patients who were not cured		
Smith 2016	Wrong outcomes		
Song 2018	Wrong intervention. Enhanced SCP vs SCP		
Stanciu 2015	Wrong intervention		
Strand 2011	Wrong outcomes		
Van Rhijn 2011	Wrong patient population		
Verberne 2015	Stepped wedge/cross-over design		
Visser 2015	Wrong intervention. Comparing 1 group consultation to 1 individual visit		
Watson 2014	Wrong intervention		
Wheelock 2015	Wrong outcomes		

**SCP:** survivorship care package(s)



## **Characteristics of ongoing studies** [ordered by study ID]

В	ierrin	g 2016

Trial name or title	Comparison of standard follow-up and intensive PET/CT and EUS based follow-up in patients having radical surgery for pancreas and gastric cancer. A randomised controlled study
Methods	Randomised trial
Participants	Patients R0-resected for pancreatic or gastric cancer
Interventions	Standard clinical follow-up at 3, 6, 9, 12, 18 and 24 months postoperatively Follow up with PET/CT and endosonography at the same intervals
Outcomes	<ul> <li>Detection of asymptomatic recurrences</li> <li>Mortality</li> </ul>
Starting date	March 2011
Contact information	Center for Surgical Ultrasound, Odense University Hospital, Denmark
Notes	Data collection was reported to be completed in 2016.

### Duineveld 2015

Trial name or title	Improving care after colon cancer treatment in The Netherlands, personalised care to enhance quality of life (I CARE study): study protocol for a randomised controlled trial
Methods	Multi-centre 2 x 2 factorial randomised trial
	n = 300
Participants	Patients with stage I, II, or III colon carcinoma
Interventions	(Usual follow-up visits and aftercare provided in secondary care
	<ul> <li>Usual follow-up visits and aftercare provided in secondary care with additional use of Oncokom- pas</li> </ul>
	Follow-up and aftercare in primary care
	Follow-up and aftercare in primary care with additional use of Oncokompas
Outcomes	• QoL
	Physical outcomes and psychosocial outcomes
	<ul> <li>Number of investigations, referrals and related communication between secondary and primary care</li> </ul>
	<ul> <li>Time to detection of recurrence detection and protocol adherence</li> </ul>
	Attention to preventive care
	Self-management of participants
	Patient satisfaction
	Preference of care at the end of the trial
Starting date	Not reported



Duineveld 2015 (Continued)	
Contact information	Academic Medical Centre, Department of Primary Care, University of Amsterdam, Meibergdreef 9, 1105, AZ, Amsterdam, The Netherlands. l.a.duineveld@amc.uva.nl
Notes	Recruitment of participants started in April 2015. Data collection is reported to last for 60 months.
zendam 2018	
Trial name or title	ENdometrial cancer SURvivors' follow-up carE (ENSURE): less is more? Evaluating patient satisfaction and cost-effectiveness of a reduced follow-up schedule: study protocol of a randomised controlled trial
Methods	A national multicenter (non-inferiority) randomised trial in 46 hospitals throughout the Netherlands
Participants	N = 282
	Patients with stage 1A and 1B low-risk endometrial cancer, for whom adjuvant radiotherapy is not indicated after initial surgery. At 6, 12, 36, and 36 months the participant will receive a questionnaire plus pre-stamped envelope at their home address.
Interventions	<ul> <li>Intervention arm: he follow-up schedule will be limited to 4 follow-up visits at 3, 12, 24, and 36 months, under the specific condition that patients have easy and prompt access to care (specialised nurse of gynecologist) if symptoms or questions occur.</li> <li>Control arm: the control group receives follow-up care according to Dutch guidelines. This guide line proposes follow-up visits every 3–4 months during the first and second years, every 4–6 months during the third year, and every 12 months during the 4th and 5th years after the end of treatment irrespective of stage and grade, resulting in a total of 10–13 visits in 5 years.</li> </ul>
Outcomes	<ul> <li>Patient satisfaction</li> <li>Cost-effectiveness</li> <li>Health-care use</li> <li>Health-related quality of life (EORTC QLQ-C30 and EORTC QLQ-EN24)</li> <li>Worry including fear of recurrence (IOCv2)</li> <li>Illness perception (BIPQ)</li> <li>Anxiety and depression (HADS)</li> <li>Satisfaction with information provision (EORTC-INFO25)</li> <li>Time to recurrence</li> <li>Survival</li> </ul>
Starting date	September 2015. Currently recruiting
Contact information	Nicole Ezendam, PhD, The Netherlands Comprehensive Cancer Organisation, n.ezendam@iknl.nl
Notes	Estimated study completion date: December 2022
avales 2015	
Trial name or title	Health and economic outcomes of two different follow up strategies in effectively cured advanced head and neck cancer
Methods	Randomised, multicentre trial to evaluate the cost-effectiveness of 2 different follow-up programmes in head and neck cancer survivors
ollow-up strategies following	completion of primary cancer treatment in adult cancer survivors (Review)



Favales 2015 (Continued)	n = 330
Participants	Head and neck cancer patients deemed to be in complete remission at month 6 (+/- 1 month) after curative treatment
Interventions	<ul> <li>Arm A (non-intensive): follow-up according to National Comprehensive Cancer Network guide- lines, consisting of outpatient visits according to the schedule foreseen for single head and neck subsite. At each follow-up visit the participants will report all new symptoms and they will receive both physical and fibre optic endoscopic head and neck examination.</li> </ul>
	<ul> <li>Arm B (intensive): follow-up outpatient visits will be performed similarly to Arm A, including physical and fibre optic endoscopic head and neck evaluation and laboratory tests and questionnaires. Locoregional imaging will be requested for all the participants twice/year in the first 2 years and once/year in the 3rd and 4th year; PET scan will be requested yearly in the first 3 years.</li> </ul>
Outcomes	The most cost-effective follow-up strategy
	<ul> <li>Percentage of potentially salvageable recurrences or second primaries</li> </ul>
	Cause-specific survival
	<ul> <li>Overall survival of participants recurring in both groups of follow-up approach</li> </ul>
Starting date	June 2014
Contact information	Paolo Bossi, MD Tel: +39 022390 ext 2765 paolo.bossi@istitutotumori.mi.it
Notes	Recruitment of participants was still ongoing as of June 2016. Data collection is reported to last for 5 years.

### **FURCA 2017**

ORCA 2011	
Trial name or title	Follow-up after rectal cancer: developing and testing a novel patient-led follow-up program. Study protocol
Methods	Multicentre randomised trial in 4 Danish colorectal surgical departments in Aarhus, Randers, Herning and Aalborg
Participants	N = 334
	Patients > 18 years of age, surgical resection for primary adenocarcinoma in the rectum (0–15 cm from the anal verge, determined by endoscopy); pathologically verified R0/R1 resection
Interventions	<ul> <li>Intervention arm: participants in the experimental arm were enrolled in a patient-led follow-up program, based on patient-education and self-referral.</li> <li>Control arm: patients with sphincter-preserving resection receive outpatient visits including rectoscopy at 6, 12, 18, 24 and 36 months. Patients with rectal amputation and a permanent stoma receive outpatient visits at 3, 12 and 36 months access to stoma care by specialist nurses.</li> <li>All patients receive CEA and CT of the chest, abdomen and pelvis at 1 and 3 years after surgery perioperative clean colon colonoscopy, and then every 5 years until the age of 75 years.</li> </ul>
Outcomes	<ul> <li>HRQoL</li> <li>Bowel function</li> <li>Stoma function</li> <li>Urinary function</li> <li>Sexual function</li> <li>Chronic pain</li> <li>Fatigue</li> </ul>



• • • • • •	Fear of cancer recurrence Psychological distress Self-efficacy Patient involvement in healthcare Patient information and sense of security Cost-benefit -QALYs February 2016 Hovdenak Jakobsen, Aarhus University Hospital, Aarhus, Denmark, idajak@rm.dk
•	Self-efficacy Patient involvement in healthcare Patient information and sense of security Cost-benefit -QALYs February 2016
•	Patient information and sense of security  Cost-benefit -QALYs  February 2016
	Cost-benefit -QALYs February 2016
	February 2016
Starting date 26	Hovdenak Jakobsen, Aarhus University Hospital, Aarhus, Denmark, idajak@rm.dk
Contact information Ida	
Notes Est	imated study completion date: 31 August 2021
Hojo 2015	
	ensive vs. standard post-operative surveillance in high-risk breast cancer patients (INSPIRE):
	pan Clinical Oncology Group Study JCOG1204
Methods Ra	ndomised trial
n =	: 1500
	Histologically proven breast cancer confirmed by biopsy or pathological examination of the resected tumour
	No macroscopic or microscopic residual tumour by total or partial mastectomy performed within 84 days before registration
•	Axillary lymph node status, confirmed by axillary resection or sentinel lymph node biopsy
•	No distant metastases found within 168 days before registration
•	ER status and HER2 status are already determined
	No bilateral breast cancer
	Able to undergo the examinations in each arm specified in the protocol
•	Woman aged 20–70 years old
	Standard follow-up: mammography and tumour marker (CEA, CA15-3) once a year, plus routine physical examination (every 3 months for the first 3 years, every 6 months for the next 2 years, and every year afterwards)
•	Intensive follow-up: mammography and routine physical examination (same schedule as stan-
	dard follow-up); tumour marker (CEA, CA15-3) every 3 months for the first 3 years, every 6 months
	for the next 2 years; chest CT, abdomen CT, bone scintigraphy, brain MRI/CT twice a year for the first 3 years and every year for the next 2 years
Outcomes •	Overall survival
•	Disease-free survival
•	Relapse-free survival
	Distant metastasis-free survival
	Overall survival of intrinsic subtypes
	Actual number of implemented examinations
	Compliance of prespecified examinations Adverse events
Starting date No	vember 2013



lojo 2015 (Continued)	
Contact information	Hiroji Iwata, Aichi Cancer Center Hospital, Department of Breast Oncology, 1-1, Kanokoden, Chikusa-ku, Nagoya 464-8661, Japan, Tel.052-762-6111ext.3112, hiwata@aichi-cc.jp
Notes	The following was reported: participant accrual was started in November 2013. A total of 1700 participants will be enrolled for 3 years and followed up for 7 years after closure of accrual.
lefford 2017	
Trial name or title	SCORE: shared care of colorectal cancer survivors: protocol for a randomised controlled trial
Methods	A multisite randomised trial conducted at the Peter MacCallum Cancer Centre, Royal Melbourne Hospital, Western Health, St Vincent's Hospital and Austin Health, Melbourne, Victoria, Australia. Participants will complete questionnaires at 3 time points over a 12-month period (baseline and at 6 and 12 months)
Participants	N = 100
	A confirmed diagnosis of colon or rectal cancer
	Stage I-III disease
	Must have completed treatment with curative intent within the previous 3-months
	• > 18 years of age
	<ul><li>Able to read and write English</li><li>Has a GP willing to participate in the study</li></ul>
Interventions	<ul> <li>Intervention arm: a shared care model where 2 of the 4 routine hospital visits in the year after end of treatment (EOT) are replaced by GP visits (30 minutes) at the 3 and 9-month post EOT. An additional GP visit at 2 weeks post-EOT is included to discuss the follow up plan and establish common ground about the model of shared care. The following core elements will support shared care:</li> <li>SCP tailored to each participant by the research team, which may include a nurse, research assistant and/or data manager and comprises a summary of the participant's diagnosis of treatment, recommendations for follow-up and strategies to remain well. The participant and GP</li> </ul>
	<ul> <li>will receive copies.</li> <li>GP clinical management guidelines. Guidelines are in line with the Australian Cancer Network Colorectal Cancer Guidelines and recommendations from the American Cancer Society of Clinical Oncology and include guidance about tests to detect recurrence, possible late and long term effects of treatments and how to manage these, as well as how to re-refer participants to a rapid review clinic.</li> </ul>
	<ul> <li>Assessment will be based on issues frequently encountered by cancer survivors (e.g. fatigue fear and cancer recurrence) and issues experienced by colorectal cancer survivors (e.g. bowe disturbance, sexual problems).</li> </ul>
	<ul> <li>Control arm: usual care consists of 4 routine, hospital-based visits and includes taking patient history, performing a physical examination and blood tests for CEA testing at 3, 6, 9 and 12-months post-end of treatment</li> </ul>
Outcomes	<ul> <li>Overall QoL (EORTC QLQ-C30 and CR29)</li> <li>Unmet needs (Short-Form Survivor Unmet Needs Survey)</li> <li>Continuity of care (Picker Ambulatory Oncology survey)</li> <li>Satisfaction (PSQ – short form)</li> <li>Cost benefit analysis</li> </ul>
Starting date	February 2017
Contact information	Michael Jefford, Peter MacCallum Cancer Center, Austialia



Jefford 2017 (Continued)	Michael.Jefford@petermac.org
Notes	Date of last data collection estimated to be September 2019
KRONOS 2017	
Trial name or title	Three-monthly dynamic evaluation of CEA and CA15-3 and 18-FDG PET vs usual practice in the follow-up of early breast cancer patients: a prospective, multicenter, randomised trial (KRONOS >= Patient-Oriented New Surveillance-Study Italy)
Methods	Multisite randomised trial in 7 hospitals in Italy
Participants	N = 800
	Patients diagnosed with stage I-III breast cancer, who underwent adequate surgery are eligible.
	The study includes patients at the beginning of the follow-up after the conclusion of primary treatment (cohort 1), and patients that have concluded without relapse the first 5 years of follow-up (cohort 2).
Interventions	Eligible participants will be randomised in a 1:1 ratio to follow-up according to local practice (control arm) or to 3-monthly serial dosing of CEA and CA15.3 and subsequent imaging studies (18-FDG PET) only in case of an increase of CEA and/or CA 15.3 > a critical difference (CEA +100% and/or CA15.3 +75%) compared to baseline.
Outcomes	<ul> <li>Time interval between date of randomisation and date of diagnosis of disease distant recurrence</li> <li>PPV and NPV of CEA and CA15.3</li> <li>Diagnostic anticipation in the different subtypes (ER and HER2 status)</li> <li>How many imaging diagnostic tests will be avoided in the experimental arm compared to the control arm</li> <li>QoL</li> </ul>
Starting date	October 2014. Currently recruiting
Contact information	Claudio Zamagni MD, Azienda Ospedaliero-Universitaria di Bologna zamagniclaudio.sper@aosp.bo.it
Notes	The follow-up will continue until 10 years from surgery.
Lepage 2015	
Trial name or title	Effect of 5 years of imaging and CEA follow-up to detect recurrence of colorectal cancer: the FFCD PRODIGE 13 randomised phase III trial
Methods	A co-operative parallel randomised prospective multicentre phase III trial
	n = 1925
Participants	<ul> <li>Patients &gt; 18 years</li> <li>Pathologically confirmed adenocarcinoma of the colon or the rectum</li> <li>Stage II or III disease</li> <li>No distant metastatic disease</li> <li>CEA ≤ 1.5 x ULN after surgery</li> </ul>



Lepage 2015 (Continued)	<ul> <li>WHO performance status 0-1</li> <li>Not pregnant or nursing</li> <li>Fertile participants must use effective contraception</li> <li>No inflammatory bowel disease</li> <li>No other malignancy within the past 5 years except basal cell carcinoma of the skin and/or carcinoma in situ of the cervix</li> <li>No genetic syndromes</li> </ul>
Interventions	<ul> <li>In the standard monitoring arm, abdominal US examination is performed every 3 months for 3 years, then every 6 months for 2 years, then annually. A CXR is performed every 6 months for 3 years then annually for 2 years.</li> <li>In the intensive monitoring arm, a thoraco-abdominal-pelvic CT scan alternating with abdominal US is performed every 3 months for 3 years, then every 6 months for 2 years. CEA levels are measured every 3 months for 3 years, then every 6 months for 2 years.</li> </ul>
Outcomes	<ul> <li>5-year overall survival</li> <li>Disease-free survival</li> <li>Resection rates after recurrence</li> <li>Survival rates after recurrence resection</li> <li>QoL</li> <li>Cost-effectiveness</li> </ul>
Starting date	September 2009
Contact information	Come Lepage, Centre Hospitalier Universitaire de Dijon
Notes	Estimated study completion date is December 2020.

### Mathiesen 2014

Trial name or title	Follow-up of endometrial cancer patients (OPAL)
Methods	Parallel randomised trial
	n = 211
Participants	Women ≥ 18 years diagnosed with stage I endometrial cancer
Interventions	No Intervention: follow-up. Participants in this arm attend regular follow-up examinations, as is the current standard, at the department of gynaecology following surgery
	<ul> <li>Experimental: self-referral. Instead of regular follow-up examinations, this group is carefully in- structed in alarm symptoms that require contact with a physician. Intervention: other. Instruction in self-referral</li> </ul>
Outcomes	<ul> <li>Fear of cancer recurrence</li> <li>QoL</li> <li>Disease-specific QoL</li> <li>Post-traumatic growth</li> <li>QALYs</li> <li>Unmet needs</li> <li>Disease-free survival</li> <li>Incidence of disease recurrence</li> <li>Resource use at hospital, primary care and use of medicinal products</li> </ul>



Mathiesen 2014 (Continued)	Resource use at hospital
Starting date	May 2013
Contact information	Mette M Mathiesen, Department of Gynecology, Odense University Hospital
Notes	Recruitment completed. Estimated study completion date is April 2019.

### NCT01450020

Trial name or title	Peer navigator education in improving survivorship care in African American breast cancer survivors
Methods	Randomised trial at City of Hope Medical Center, California, USA, investigating the addition of an education intervention based on PN to usual care
Participants	N = 145
	Patients aged ≥ 18 years who self-identifies as African-American, 1-12 months post completion of treatment for stage 0-3 breast cancer
	Receiving health care primarily through a health maintenance organisation (HMO)
Interventions	Arm 1: participants receive 4 PN sessions tailored to their needs followed by a 6-month booster session and ACS materials.
	Arm 2: participants receive ACS materials.
Outcomes	<ul> <li>Understanding of survivorship care planning</li> <li>Adherence to SCP</li> <li>Physical and health-related QoL</li> <li>Preparedness for life as a new survivor</li> </ul>
Starting date	1 June 2012
Contact information	Kimlin Ashing-Giwa, City of Hope Medical Center, kashing@coh.org
Notes	Estimated study completion date: July 2019

## NCT02261389

TCT OZZOS	
Trial name or title	Follow-up of early breast cancer by dynamic evaluation of CEA and CA 15.3 followed by 18FDG-PET
Methods	Parallel randomised trial
	n = 800
Participants	Male or female ≥ 18 years
	Histologically confirmed stage I-III epithelial breast cancer
	Adequate surgery of breast and axilla:
	participants must have undergone either a total mastectomy or breast-conserving surgery



NCT02261389 (Continued)	surgical margins of the resected specimen must be histologically free of invasive tumour
Interventions	<ul> <li>Arm A, no intervention: usual follow-up practice. Imaging studies and serum markers (CEA, CA 15.3, others) performed according to local practice</li> <li>Arm B, experimental: assessment of tumour markers. Serum CEA and CA 15.3 performed every smonths</li> </ul>
	No imaging studies allowed in asymptomatic patients: imaging studies (18-FDG-PET) performed only in case of critical increase of CEA and /or CA 15.3 serum levels (+ 100% for CEA and + 75% for CA15.3), even if in the normal range.
Outcomes	<ul> <li>Time interval between date of randomisation and date of diagnosis of disease distant recurrence</li> <li>Predefined critical difference of CEA and CA15-3</li> <li>Exploratory analysis in the different subtypes</li> <li>Imaging diagnostic tests evaluation</li> <li>Patient QoL evaluation</li> </ul>
Starting date	September 2014
Contact information	Claudio Zamagni, 051 2144548 ext +39, zamagniclaudio.sper@aosp.bo.it
Notes	Study is recruiting. Estimated study completion date is September 2022.
Trial name or title	Individualised versus conventional medical follow-up for women after primary treatment for ovarian cancer
Methods	an cancer  2-arm randomised trial
	n = 113
Participants	Diagnosis of ovarian cancer (includes fallopian tube and peritoneal cancers)
	Within 1 month of completion of primary treatment including surgery and chemotherapy/radio-therapy or surgery alone, irrespective of outcome with regard to remission
	Expected survival ≥ 3 months
	≥ 18 years
Interventions	<ul> <li>No intervention: conventional follow-up/treatment as usual involving 1 post-treatment appoint ment then 3 monthly appointments with a doctor. At appointments:         <ul> <li>medical history</li> <li>investigations to monitor disease progression including CA125 tumour marker blood test if this were raised at diagnosis</li> <li>a physical examination may be performed.</li> </ul> </li> <li>Experimental: individualised follow-up delivered by a nurse. Frequency and type (telephone o face-to-face) is negotiated to suit participants' individual situation. Assessment by holistic guide The intervention is informed by a model of health promoting interactions oriented towards im proving self-efficacy. The nurses will provide information and support to help participants man age symptoms and psychological discomfort</li> </ul>
Outcomes	<ul> <li>HRQol and disease-specific QoL 3, 6, 12,18, and 24 months</li> <li>Anxiety and depression</li> <li>Patient Satisfaction</li> </ul>



NCT02298855 (Continued)	
Starting date	January 2006
Contact information	Anne Lanceley, University College, London
Notes	Study is reported to be completed in the last update posted November 2014

#### NCT02637349

Trial name or title	Polaris oncology survivor transition (POST) System
Methods	A single blind, randomised trial to test whether the SCPs created with the Polaris Oncology Survivorship Transition (POST) web-based system impact patient and provider outcomes.
Participants	N = 230 patients ≥ 18 years, confirmed diagnosis of breast cancer (not metastatic), a final active treatment appointment scheduled with oncology team
Interventions	<ul> <li>Experimental: POST SCP. Participant receives SCP after active treatment ends. It will be discussed with the participant. SCP includes medical and psychosocial history, medical contact informa- tion, 5-year follow-up plan and educational materials.</li> </ul>
	Active comparator: POST TAU. Participant receives treatment as usual after active treatment ends
Outcomes	• QoL
	Depression and anxiety
	Adherence to medical and behavioural health recommendations
	Health care utilisation
	Patient and provider
Starting date	November 2016
Contact information	Erin O'Hea, University of Massachusetts Medical School – Cancer Center, erin.ohea@umassmed.edu
Notes	

10102555520	
Trial name or title	A study on optimizing follow-up for postmenopausal women with breast cancer treated with adjuvant endocrine therapy
Methods	Parallel randomised trial
	n = 200
Participants	<ul> <li>Postmenopausal at the time of diagnosis (menostasis &gt; 12 months. Bilateral salpingo-oophorectomy)</li> </ul>
	<ul> <li>Complete disease remission after primary operation</li> </ul>
	<ul> <li>Histologically confirmed hormone-receptor positive breast cancer, ≥ 1% of the tumour cells express hormone receptors</li> </ul>
	<ul> <li>High-risk profile with a 10-year recurrence of &gt; 10%</li> </ul>
	<ul> <li>Planned adjuvant endocrine therapy regardless of other adjuvant therapy to be initiated within 1 month or initiated within the last 9 months</li> </ul>



NCT02935920 (Continued)	Women 45-95 years
Interventions	<ul> <li>No intervention: standard follow-up:         <ul> <li>scheduled clinical examination every 6 months throughout the course of adjuvant treatment</li> <li>performed by a doctor or nurse</li> </ul> </li> <li>Experimental: individual, tailored follow-up</li> </ul>
	Participant symptoms are evaluated by the use of PRO-data to uncover the needs of a consultation. The outcome of the questionnaire is used to customise the follow-up programme to the individual participant. Individualised follow-up in the context of shared decision making, with the use of PRO-data to evaluate the participant needs of consultations.
Outcomes	<ul> <li>PREM up to 2 years</li> <li>Resources spent on individualised follow-up based on PRO-data and standard follow-up</li> <li>CollaboRATE-score between the individualised and standard follow-up</li> <li>HRQoL</li> <li>Issues of importance and concern to postmenopausal woman with breast cancer in adjuvant endocrine therapy during follow-up after primary treatment</li> <li>Evaluation of current information level during primary treatment</li> </ul>
Starting date	April 2016
Contact information	Cathrine L. Riis, Department of Oncology, 7100 Vejle, Region of Southern Denmark, cathrine.lundgaard.riis@rsyd.dk
Notes	Study is recruiting. Estimated study completion date December 2019

Trial name or title	MyHealth: follow-up after breast cancer treatment (MyHealth)
Methods	Parallel randomised trial
	n = 494
Participants	Complete remission following primary treatment for loco-regional breast cancer (stage I-II) - no confirmed genetic predisposition to breast cancer
	<ul> <li>Female</li> <li>Performance status ≤ 3</li> </ul>
	• ≥ 40 years
Interventions	<ul> <li>No intervention: MyHealth control condition</li> <li>Physician-led follow-up</li> <li>Regular visit with physician every 6 months</li> <li>Experimental: MyHealth intervention arm</li> <li>Nurse-led follow-up</li> </ul>
	The MyHealth intervention is a nurse-led individually tailored symptom management programme, focused on patient education and regular collection of PRO subsequently evaluated by specialist nurses and navigation to health care service. The nurse will meet with the participant on 3-5 planned appointments focused on adjustment of life after breast cancer treatment including information on symptoms of relapse or late effects and how to react on these. Close relatives are invited if participants accept. Participants will report PROs on symptoms of recurrence and late effects every 3 months during the 1st year and thereafter every 6 months. The appointments with the nurse are finalised within 3-6 months and participants will be followed with PRO for 3 years.



### NCT02949167 (Continued)

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- Breast cancer-specific symptom burden up to 5 years after primary treatment
- Patient activation
- Anxiety and depression
- Self management
- Fear of recurrence
- Work ability
- QALY
- Health care use

Starting date	November 2016
Contact information	Lena Saltbaek, Department of Oncology and Palliative Care, Naestved Hospital, Ringstedvej 61, 4700 Naestved. +45 56513260. lsal@regionsjaelland.dk
Notes	Study is recruiting. Estimated study completion date May 2021

Trial name or title	PC 360 survivorship (prostate cancer survivorship 360°)
Methods	A randomised trial to evaluate whether a personalised prostate cancer SCP intervention is more effective than usual care on patient activation (primary outcome) and access to services, self-management support, satisfaction with information, HRQoL and cancer worry (secondary outcomes). Carried out at 3 Canadian prostate centres
Participants	N =180 men with histologically confirmed localised (T1-T3N0M0) prostate cancer, age at diagnosis > 18 years, treated with curative intent, treatment received > 1 month and < 6 months, disease-free as defined by absence of somatic disease activity parameters as per oncologist/urologist
Interventions	<ul> <li>Intervention arm: SCP is comprised of a 30-min, nurse-led, face-to-face intervention and the provision of a tailored prostate cancer-specific SCP. Persistent effects and concerns that are identified will prompt the development of a tailored management plan captured within the prostate cancer SCP. Relevant patient education materials will be linked electronically. Nurses will use motivational interviewing techniques to effect increase healthy behaviours and empower the prostate cancer survivor to actively self-manage persistent treatment effects and to decrease their risk of late effects by providing effective health information, support, and self-management support.</li> <li>Usual care arm: this usually involves a brief office visit (approximately 5-10 min) with pertinent history and physical examination related to surgical/radiation recovery, review of the pathology and general instructions regarding the next step in follow-up.</li> </ul>
Outcomes	<ul> <li>Patient activation (primary outcome)</li> <li>Service utilisation</li> <li>Self-management</li> <li>Satisfaction with information</li> <li>HRQoL and cancer worry</li> </ul>
Starting date	May 2017
Contact information	Jennifer M Jones, PhD, Princess Margaret Cancer Centre, University Health Network, jennifer.jones@uhn.ca
Notes	Estimated study completion date: September 2019



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Trial name or title	A randomised trial to assess the role of imaging during follow up after radical surgery of high risk melanoma
Methods	Multicentre trial in 21 Swedish hospitals. Participants are randomised 1:1 to routine follow-up for 3 years with regular doctors' appointments according to national guidelines and the same follow-up but with the addition of whole-body CT or PET scans and blood tests.
Participants	N = 1300, ≥ 18 years, radical surgery for cutaneous malignant melanoma (CMM) stage IIb-c and III, sufficient renal function for IV contrast scannings
Interventions	<ul> <li>Experimental arm:         <ul> <li>CT or PET scans</li> </ul> </li> <li>Scans and blood tests are scheduled at baseline, months 6, 12, 24 and 36</li> <li>Control arm: routine follow-up according to national guidelines</li> </ul>
Outcomes	<ul> <li>5-year survival</li> <li>QoL</li> <li>Depression and anxiety</li> </ul>
Starting date	June 2017. Currently recruiting
Contact information	Gustav Ullenhag, Uppsala University Hospital, gustav.ullenhag@igp.uu.se
Notes	Estimated study completion date: 31 December 2026

Trial name or title	Shared care: patient-centered management after hematopoietic cell transplantation
Methods	Multicentre randomised trial at 9 centres in USA to evaluate the effectiveness of allowing patients who have had a HCT to receive some of their post-transplant care with a local oncologist rather than returning to the transplant centre for all of their follow-up
Participants	N = 408, ≥ 18 years, scheduled to receive an allogeneic HCT at the Dana-Farber Inpatient Hospital under the care of a Dana-Faber Cancer Institute physician, residence in New York, Maine, New Hampshire, Vermont, Connecticut, or Massachusetts. Referred from or live < 1 hour from 1 of the local participating centres
Interventions	Experimental: shared care  For the first 90 days, participants alternate between local oncologist and Dana-Faber Cancer Insti-
	tute for weekly visits.
	From 90 to 180 days, participants alternate between local and Dana-Faber Cancer Institute every 2-3 weeks.
	Usual care: participants receive all follow-up care at Dana-Faber Cancer Institute only, which is currently the standard care.
Outcomes	• QoL
	Financial hardship
	100-day non-relapse mortality
	2-year overall survival



NCT03244826 (Continued)	chronic graft versus host diesease (cGVHD)
Starting date	January 2018
Contact information	Gregory A. Abel, Dana-Farber Cancer Institute, Gregory_Abel@dfci.harvard.edu
Notes	Estimated study completion date: 31 December 2022

## NCT03328247

Trial name or title	Achieving self-directed integrated cancer aftercare (ASICA) in melanoma						
Methods	Randimised trial in the UK investigating whether a digital app (ASICA) in addition to routine follow-up can help people with melanoma to do more regular and effective total-skin-self-examinations, and whether this would lead to earlier detection of recurrent and new primary melanomas.						
Participants	N = 240 adults (≥ 18), treated for stage 0-2C cutaneous melanoma within the preceding 24 months						
Interventions	<ul> <li>Experimental arm: ASICA app in addition to routine follow-ups</li> <li>Control arm: routine melanoma follow-ups</li> </ul>						
Outcomes	<ul> <li>Cancer worry (Melanoma Worry Scale)</li> <li>Anxiety and depression (HADS)</li> <li>QoL (EQ-5D-5L)</li> <li>Detection of recurrence</li> <li>Adherence and self-efficacy in carrying out total-skin-self-examinations</li> </ul>						
Starting date	Estimated start January 2018						
Contact information	Peter Murchie, University of Aberdeen, p.murchie@abdn.ac.uk						
Notes	Results are expected in March 2020 (email from study author)						

Trial name or title	Randomised multicentric comparative study between a conventional and an intensive follow up strategy after treatment of a head and neck squamous cell carcinoma (SURVEILL'ORL)						
Methods	Randomised trial in France to compare the efficacy in terms of overall survival of 2 follow-up strategies (conventional vs intensive) among smokers and/or alcohol drinkers.						
	Patients, > 35 year, in complete remission 2-4 months after treatment of head and neck squamous cell carcinoma						
Participants	N = 1080, men or women > 35 years, current or previous smokers (smoked > 10 packs year) or alcohol drinkers (current or previous, > 140 g alcohol/week) or both, histologically proven invasive HNSCC stage 0-IVa, excluding T4b and nasopharynx. Patients with in situ carcinoma are eligible, treated with curative intent free of cancer at the post-treatment clinical and radiological examination (negative PET-CT for N ≥ 2) at least 2 months after the end of the last treatment and no later than 4 months after.						
Interventions	<ul> <li>Intensive arm: adding to the conventional follow-up strategy, an annual head and neck and tho- racic injected CT-scan and Lugol upper gastrointestinal endoscopy (the first performed 12 months</li> </ul>						



#### NCT03519048 (Continued)

after inclusion), annual whole body PET-CT (the first at 6 months after inclusion). These 3 exams are performed every year for 3 years after inclusion (i.e. 3 CT-scans, 3 digestive endoscopies and 3 PET-CTs per participant). Clinical follow-up will be conducted as in the conventional follow-up group and panendoscopy or bronchoscopy will be performed if needed. After 3 years, participants will be followed by conventional follow-up.

Comparison arm: clinical examination with nasofibroscopy every 1-3 months first year post-treatment, every 2-4 months second year, every 4-6 months third year (mean of around 13 visits) and every 6 months thereafter. Low-dose chest CT scan every year in participants with tobacco consumption history of > 20 pack-year. Panendoscopy plus CT-scan are performed in case of clinical symptoms or abnormal clinical exam.

Outcomes	Overall survival (5 years)
Starting date	January 2018
Contact information	Stephane Temam, MD, Gustave Roussy, Cancer Campus, Paris, stephane.temam@gustaveroussy.fr
Notes	Estimated completion date: January 2031

Trial name or title	A research study of patient-led surveillance compared to clinician-led surveillance in people treated for localised melanoma (MEL-SELF)					
Methods	Pilot randomised trial in 3 centres in Australia evaluating digitally supported skin self-examination compared to usual care in people treated for localised melanoma					
Participants	N = 100, aged ≥ 18 years, have been treated for stage 0/I/II melanoma and are attending regular melanoma surveillance follow-ups at the Melanoma Institute Australia (MIA), Royal Prince Alfred Hospital (RPAH) or the Newcastle Skin Check Clinic					
Interventions	Experimental arm: participants will perform self-surveillance of the skin using a dermatoscope device. They will receive guidance from the ASICA skin checker and receive reminders every 2 months to perform self-examination. They will receive an educational booklet, <i>Your guide to early melanoma</i> and scheduled visits to their clinician as required.					
	Control arm: participants will receive an educational booklet <i>Your guide to early melanoma</i> and scheduled visits to their clinician as required.					
Outcomes	<ul> <li>Participation rate</li> <li>Adherence to guidelines on skin examination</li> <li>Fear of recurrence</li> <li>Anxiety, stress, depression</li> <li>Number of lesions surgically evaluated</li> <li>Patient knowledge, confidence, attitude towards skin self-examination</li> <li>Resource use</li> </ul>					
Starting date	July 2018					
Contact information	Katy Bell, University of Sydney, katy.bell@sydney.edu.au					
Notes	Estimated study completion date: December 2019					



Trial name or title	Surveillance with PET/CT and liquid biopsies of stage I-III lung cancer patients after completion of definitive therapy							
Methods	A multicenter, randomised trial in Denmark to:							
	<ul> <li>assess if surveillance with whole body PET combined with CT (PET/CT) including the brain can increase the number of treatable relapses</li> </ul>							
	<ul> <li>concurrently collect liquid biopsies for later analysis, potentially enabling even earlier and minimally invasive detection and characterisation of relapse.</li> </ul>							
Participants	N = 750, patients with NSCLC, proven by cytology or histology							
	Patient in clinical stages I-III,							
	• Age ≥ 18 years							
	<ul> <li>Performance status ≤ 2 at the time of referral to therapy</li> </ul>							
	<ul> <li>Patient referred for definitive treatment (e.g. surgery, surgery followed by adjuvant chemother- apy, concomitant radio-chemotherapy, conventional or stereotactic radiotherapy or radiofre- quency ablation)</li> </ul>							
Interventions	<ul> <li>Experimental arm:</li> <li>8F-2-fluoro-2-deoxy-D-glucose fluorodeoxyglucose PET with CT (FDG PET/CT) replacing CT at months 6, 12, 18 and 24, otherwise control with CT scan months 9, 15 and 21.</li> </ul>							
	<ul> <li>QoL assessment and liquid biopsy every 3 months for later analysis</li> </ul>							
	Control arm:							
	<ul> <li>CT scan and clinical evaluation every 3 months</li> </ul>							
	<ul> <li>QoL assessment and liquid biopsy at every 3 months for later analysis</li> </ul>							
Outcomes	Number of relapses treatable with curative intent							
	Time to relapse							
	Overall survival (3 years)							
	Performance status at relapse							
	• QoL							
	<ul> <li>Adverse events</li> <li>Cost-effectiveness</li> </ul>							
	Cost-enectiveness							
Starting date	October 2018							
Contact information	Mette Poehl, Rigshospitalet, Denmark, mette.poehl@regionh.dk							
Notes	Estimated study completion date: October 2023							

## Taylor 2016

Trial name or title	Protocol for care after lymphoma (CALy) trial: a phase II pilot randomised controlled trial of a lymphoma nurse-led model of survivorship care
Methods	Pilot study, phase II randomised clinical trial
Participants	<ul> <li>Pathologically confirmed new diagnosis of Hodgkin's lymphoma or non-Hodgkin's lymphoma</li> <li>Completed first-line curative intent chemotherapy or second-line curative intent autologous stem cell transplant within the previous 3 months</li> <li>No evidence of lymphoma disease on mid-treatment interim PET scan or post-treatment PET scan where these are performed</li> </ul>



Taylor 2016 (Continued)	• >19 years							
Interventions	<ul> <li>&gt; 18 years</li> <li>Control group: participants will receive follow-up care as per haematologists' usual practice at a large tertiary cancer centre in Western Australia</li> <li>Intervention group: nurse-led follow up at the lymphoma survivorship clinic that comprises 3 face-to-face appointments with delivery of tailored resources, a SCP and treatment summary. The SCP and treatment summary will be given to the participant and GP.</li> </ul>							
Outcomes	<ul> <li>Depression and anxiety</li> <li>Adjustment to cancer</li> <li>Patient empowerment</li> </ul>							
Starting date	Not reported							
Contact information	Karen Taylor; Karen.Taylor@health.wa.gov. au							
Notes	Study authors reported: "We plan to complete the study by December 2017 and report trial results in 2018."							
Turner 2014								
Trial name or title	The ENHANCES studyenhancing head and neck cancer patients' experiences of survivorship: study protocol for a randomised controlled trial							
Methods	Prospective randomised trial with 3 study arms							
	n = 120							
Participants	<ul> <li>Patients who have received treatment for head and neck cancer</li> <li>Completion of a defined treatment protocol for cancer of the tongue; mouth; salivary glands; pharynx; oro-, hypo- and/or nasopharynx; nasal cavities; middle ear; sinuses; or larynx or completion of a defined treatment protocol for non-melanoma skin cancers of the head and neck requiring treatment known to cause toxicity (for example, any 1 or combination of surgery, radiotherapy or chemotherapy)</li> <li>Possess physical, cognitive and mental status enabling participation in the study</li> </ul>							
Interventions	<ul> <li>Arm 1: Usual care: standard care and other usual supportive care measures, including medical treatments and healthcare appointments.</li> <li>Arm 2: Information in the form of a written resource: in addition to usual care, participants in this group will receive a copy of Facing the Future: Living with Confidence after Treatment for Head and Neck Cancer</li> <li>Arm 3: Head &amp;Neck Cancer Survivor Self-management Care Plan (HNCP) delivered by an oncology nurse: participants will receive an individualised HNCP within 1 month of completion of treatment. The HNCP will be developed during a face-to-face supportive and educational session between the participant and a trained nurse. The session will last up to 60 min and will be focused on developing the participant's self-efficacy to manage identified health concerns. Information will be provided about symptom management, and strategies to promote behaviour change will also be discussed. Participants will also receive a copy of the resource Facing the Future: Living with Confidence after Treatment for Head and Neck Cancer and continue to receive usual care. To facilitate consistent, ongoing support, a copy of the HNCP will be sent to the participant's GP.</li> </ul>							
Outcomes	<ul> <li>HRQoL</li> <li>Head and neck cancer-related symptoms</li> <li>Self-efficacy for coping with cancer</li> <li>Anxiety and depression</li> </ul>							



Turner 2014 (Continued)	• QALYs								
Starting date	Not reported  Patsy Yates, p.yates@qut.edu.au 3 Institute of Health and Biomedical Innovation, Queensland University of Technology, Musk Ave, Kelvin Grove, QLD 4059, Australia  Study authors reported: "Eight patients have been recruited across both sites to date (2014)"								
Contact information									
Notes									
Wang 2016									
Trial name or title  A randomised controlled study for the long term follow-up of breast cancer survi care physician (PCP) coordinated care delivery model									
Methods	Randomised trial								
Participants	Women treated for breast cancer stage 0-3								
Interventions	<ul> <li>Control arm: oncologist care</li> <li>Intervention arm: comprehensive SCP, a primary-care-physician-co-ordinated care delivery model</li> </ul>								
Outcomes	<ul> <li>Late effects of breast cancer treatment</li> <li>Anxiety and depression</li> <li>HRQoL</li> <li>Recurrence-related clinical outcome</li> <li>Preventive care</li> <li>Chronic disease management</li> <li>Patient satisfaction</li> <li>Health services utilisation</li> </ul>								
Starting date	Not reported								
Contact information	Koo Foundation Sun Yat-Sen Cancer Center, Taipei, Taiwan								
Notes	Study authors reported: "270 eligible individuals have been approached with an enrollment rate of 58% (target sample 1,200)"								
Zola 2016									
Trial name or title	Trial between two follow up regimens with different test intensity in endometrial cancer treated patients (TOTEM)								
Methods	Parallel randomised trial 4 arms								
	n = 2300								
Participants	Patients treated surgically for endometrial cancer, if in complete clinical remission confirmed by imaging stage FIGO I-IV								

• No previous or concurrent neoplasia (with the exception of carcinoma in situ of the cervix and

basalioma of the skin)



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- Other contemporaneous randomised trial may be allowed if there is not any restriction concerning follow-up
- Obtaining a written informed consent before randomisation
- Age > 18 years

#### Interventions

- Experimental 1: intensive follow-up in low-risk participants (Stage IA G1 and G2)
  - First 2 years of follow-up from the end of primary treatment: clinical visit with gynaecological exploration every 4 months; Pap tests; chest, abdomen, pelvis CT every 12 months
  - From 3rd to the 5th year of follow-up: clinical visit with gynaecological exploration every 6 months; Pap test every 12 months
- Experimental 2: intensive follow-up in high-risk participants (Stage ≥ Stage IA G3)
  - First 3 years of follow-up since the end of primary treatment: clinical visit with gynaecological exploration, CA125, trans-vaginal and abdominal US every 4 months (except in conjunction with CT); Pap smear, abdomen, pelvis CT every 12 months
  - In the 4th and 5th years of follow-up: clinical visit with gynaecological exploration, CA125, trans-vaginal and abdominal US every 6 months (except in conjunction with CT), Pap smear; chest, abdomen, pelvis CT every 12 months
- Control 1: minimalist follow-up in low-risk participants (Stage IA G1 and G2)
  - First 5 years of follow-up from the end of primary treatment: clinical visit with gynaecological exploration every 6 months
- Control 2: minimalist follow-up in high-risk participants (Stage ≥ IA G3)
  - First 2 years of FU since the end of primary treatment: clinical visit with gynaecological exploration every 4 months; chest, abdomen, pelvis CT every 12 months
  - From the 3rd to the 5th year of surveillance: clinical visit with gynaecological exploration every 6 months

#### Outcomes

- · Overall survival (7 years)
- Progression-free survival (7 years)
- Proportion of complications, second cancers, co-morbidity (7 years)
- Proportion of asymptomatic participants with diagnosis of relapse (7 years)
- Proportion of participants who complete the 2 different regimes of follow-up (7 years)

Starting date	September 2008
Contact information	Paolo Zola, +39 011 3131523, paolo.zola@unito.it
Notes	Study is active but not recruiting. Estimated study completion date December 2020

18-FDG PET: 8F-fluoro-2-deoxy-D-glucose positron emission tomography; ACS: American Cancer Society; BIPQ: Brief Illness Perception Questionnaire; CA125: cancer antigen 125; CA15-3: cancer antigen 15-3; CEA: carcinoembryonic antigen; CT: computed tomography; CXR: chest X-ray; EORTC-CR29: European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core; EORTC QLQ-EN24: European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core; EORTC-INFO25: European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Endometrial cancer; EORTC-INFO25: European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Cancer information; ER: estrogen receptor; EUS: endoscopic ultrasound; EQ-5D-5L: EuroQoL-5 dimensions-5 level; FIGO: International Federation of Gynecology and Obstetrics; GP: general practitioner HADS: Hospital Anxiety and Depression Scale; HCT: hematopoietic cell transplantation; HER2: human epidermal growth factor receptor 2; HRQoL: health-related quality of life; HNSCC: head and neck squamous cell carcinoma; IOCv2: Impact of Cancer scale-version 2; IV: intravenous; MRI: magnetic resonance imaging; NPV: negative predictive value; NSCLC: non-small cell lung cancer; PET/CT: positron emission tomography/computed tomography; PN: peer navigation; PPV: positive predictive value; PREM: patient-reported experience measure; PRO: patient-reported outcome; PSQ: Patient Satisfaction Questionnaire; QALY: quality-adjusted life year; QoL: quality of life; SCP: survivorship care package(s); ULN: upper limit of normal; US: ultrasound

## DATA AND ANALYSES



## Comparison 1. Non-specialist-led versus specialist-led follow-up

Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
1 Overall Survival	2		Hazard Ratio (Random, 95% CI)	1.21 [0.68, 2.15]
2 EORTC-C30 - Global health status	4	605	Mean Difference (IV, Random, 95% CI)	1.06 [-1.83, 3.95]
3 EORTC-C30 - Physical functioning	3	306	Mean Difference (IV, Random, 95% CI)	1.65 [-2.35, 5.64]
4 EORTC-C30 - Role functioning	4	605	Mean Difference (IV, Random, 95% CI)	2.36 [-2.75, 7.47]
5 EORTC-C30 - Emotional functioning	4	605	Mean Difference (IV, Random, 95% CI)	0.52 [-2.06, 3.09]
6 EORTC-C30 - Cognitive functioning	3	306	Mean Difference (IV, Random, 95% CI)	4.41 [-1.52, 10.34]
7 EORTC-C30 - Social functioning	3	306	Mean Difference (IV, Random, 95% CI)	5.39 [1.60, 9.17]
8 STAI - State anxiety subscale	3	602	Mean Difference (IV, Random, 95% CI)	-0.55 [-2.41, 1.32]
9 HADS - Anxiety subscale	5	1266	Mean Difference (IV, Random, 95% CI)	-0.03 [-0.73, 0.67]
10 HADS - Depression subscale	5	1266	Mean Difference (IV, Random, 95% CI)	0.03 [-0.35, 0.42]

Analysis 1.1. Comparison 1 Non-specialist-led versus specialist-led follow-up, Outcome 1 Overall Survival.

Study or subgroup	Less in- More in- log[Hazard Hazard Ratio tensive tensive Ratio]							Weight	Hazard Ratio			
	N	N	(SE)			IV, Ran	dom, 9	5% CI				IV, Random, 95% CI
Koinberg 2004	0	0	0.2 (0.38)			_	-				59.44%	1.22[0.58,2.57]
Wattchow 2006	0	0	0.2 (0.46)			_	+				40.56%	1.2[0.49,2.96]
Total (95% CI)						-	-	<b>-</b>			100%	1.21[0.68,2.15]
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =0, d	f=1(P=0.98); I <sup>2</sup> =0%											
Test for overall effect: Z=0.66(P=	0.51)											
		Favour	s non-specialist	0.1	0.2	0.5	1	2	5	10	Favours sp	ecialist-led



# Analysis 1.2. Comparison 1 Non-specialist-led versus specialist-led follow-up, Outcome 2 EORTC-C30 - Global health status.

Study or subgroup	Non-sp	ecialist-led	Spec	ialist-led		Mea	an Difference		Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)		Ran	idom, 95% CI			Random, 95% CI
Augestad 2013	41	81.3 (17)	44	75.9 (19.2)			+-		11.91%	5.4[-2.3,13.1]
Kimman 2011	150	78.4 (16.2)	149	77.7 (16.2)			-		34.39%	0.7[-2.97,4.37]
Kirshbaum 2017	56	69.4 (21.5)	56	75 (20.3)		-	+		11.79%	-5.6[-13.34,2.14]
Verschuur 2009	54	73 (7)	55	71 (9)			-		41.9%	2[-1.02,5.02]
Total ***	301		304				•		100%	1.06[-1.83,3.95]
Heterogeneity: Tau <sup>2</sup> =2.8; Chi	<sup>2</sup> =4.44, df=3(P=0.	.22); I <sup>2</sup> =32.49%								
Test for overall effect: Z=0.72	(P=0.47)									
			Favours	specialist-led	-50	-25	0 25	50	Favours nor	n-specialist

# Analysis 1.3. Comparison 1 Non-specialist-led versus specialist-led follow-up, Outcome 3 EORTC-C30 - Physical functioning.

Study or subgroup	Non-sp	pecialist-led	Spec	ialist-led		Me	an Difference		Weigh	t Mean Difference
	N	Mean(SD)	N	Mean(SD)		Ra	ndom, 95% CI			Random, 95% CI
Augestad 2013	41	90.6 (16.6)	44	88.8 (15)			-		23.36%	6 1.8[-4.94,8.54]
Kirshbaum 2017	56	84.7 (17.9)	56	87.2 (13)			-		28.29%	6 -2.5[-8.29,3.29]
Verschuur 2009	54	82 (8)	55	78 (9)			=		48.34%	6 4[0.8,7.2]
Total ***	151		155				•		100%	6 1.65[-2.35,5.64]
Heterogeneity: Tau <sup>2</sup> =5.92; Ch	ni²=3.74, df=2(P=	0.15); I <sup>2</sup> =46.53%								
Test for overall effect: Z=0.81	(P=0.42)									
			Favours	specialist-led	-50	-25	0	25	<sup>50</sup> Favour	s non-specialist

# Analysis 1.4. Comparison 1 Non-specialist-led versus specialist-led follow-up, Outcome 4 EORTC-C30 - Role functioning.

Study or subgroup	Non-s	pecialist-led	Spec	ialist-led		Mea	n Difference	W	eight	Mean Difference	
	N	Mean(SD)	N	Mean(SD)		Ran	dom, 95% CI			Random, 95% CI	
Augestad 2013	41	91.6 (22.1)	44	83.8 (26.5)			+-	16	6.66%	7.8[-2.55,18.15]	
Kimman 2011	150	83.4 (21.4)	149	82.9 (23.2)			-	34	4.68%	0.5[-4.56,5.56]	
Kirshbaum 2017	56	79.4 (21.3)	56	83.8 (23.4)		-		22	2.06%	-4.4[-12.69,3.89]	
Verschuur 2009	54	76 (17)	55	69 (20)			-	2	26.6%	7[0.04,13.96]	
Total ***	301		304				•		100%	2.36[-2.75,7.47]	
Heterogeneity: Tau <sup>2</sup> =12.93; C	Chi <sup>2</sup> =5.81, df=3(P	=0.12); I <sup>2</sup> =48.4%									
Test for overall effect: Z=0.91	(P=0.36)										
			Favours	specialist-led	-50	-25	0 25	50 Fa	vours nor	ı-specialist	



# Analysis 1.5. Comparison 1 Non-specialist-led versus specialist-led follow-up, Outcome 5 EORTC-C30 - Emotional functioning.

Study or subgroup	Non-s <sub>l</sub>	pecialist-led	Spe	cialist-led		Mea	n Difference		Weight	Mean Difference	
	N	Mean(SD)	N	Mean(SD)		Ran	dom, 95% CI			Random, 95% CI	
Augestad 2013	41	91.9 (15.8)	44	87.7 (16.1)			+		14.41%	4.2[-2.58,10.98]	
Kimman 2011	150	81.7 (18)	149	82.6 (16.9)			•		42.34%	-0.9[-4.86,3.06]	
Kirshbaum 2017	56	77.5 (24.4)	56	78.3 (25.6)			<del>-</del>		7.73%	-0.8[-10.06,8.46]	
Verschuur 2009	54	80 (11)	55	79 (12)			+		35.52%	1[-3.32,5.32]	
Total ***	301		304				•		100%	0.52[-2.06,3.09]	
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =	1.75, df=3(P=0.6	3); I <sup>2</sup> =0%									
Test for overall effect: Z=0.39	(P=0.69)										
			Favours	specialist-led	-50	-25	0 25	50	Favours nor	ı-snecialist	

# Analysis 1.6. Comparison 1 Non-specialist-led versus specialist-led follow-up, Outcome 6 EORTC-C30 - Cognitive functioning.

Study or subgroup	Non-sp	ecialist-led	Spec	cialist-led		Mea	an Difference		Weight	Mean Difference	
	N	Mean(SD)	N	Mean(SD)		Ran	ıdom, 95% CI			Random, 95% CI	
Augestad 2013	41	91.1 (17)	44	86.5 (22.8)			+-		26.97%	4.6[-3.91,13.11]	
Kirshbaum 2017	56	76.9 (19.6)	56	79.1 (27)			-		26.19%	-2.2[-10.94,6.54]	
Verschuur 2009	54	84 (10)	55	76 (12)			-		46.84%	8[3.86,12.14]	
Total ***	151		155				•		100%	4.41[-1.52,10.34]	
Heterogeneity: Tau <sup>2</sup> =15.07; C	Chi <sup>2</sup> =4.38, df=2(P	=0.11); I <sup>2</sup> =54.3%									
Test for overall effect: Z=1.46	(P=0.14)										
			Favours	specialist-led	-50	-25	0 25	50	Favours nor	n-specialist	

# Analysis 1.7. Comparison 1 Non-specialist-led versus specialist-led follow-up, Outcome 7 EORTC-C30 - Social functioning.

Study or subgroup	Non-s <sub>l</sub>	oecialist-led	Spec	cialist-led		Mea	an Difference	W	eight	<b>Mean Difference</b>	
	N	Mean(SD)	N	Mean(SD)		Rar	ndom, 95% CI			Random, 95% CI	
Augestad 2013	41	91.6 (17.3)	44	87 (23.8)			+	1	8.49%	4.6[-4.2,13.4]	
Kirshbaum 2017	56	86.6 (21.3)	56	85 (22.6)			-	2	1.65%	1.6[-6.53,9.73]	
Verschuur 2009	54	85 (12)	55	78 (14)			-	5	9.86%	7[2.11,11.89]	
Total ***	151		155				•		100%	5.39[1.6,9.17]	
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =	1.28, df=2(P=0.5	3); I <sup>2</sup> =0%									
Test for overall effect: Z=2.79	P(P=0.01)										
			Favours	specialist-led	-50	-25	0 25	50 Fa	vours nor	n-specialist	



# Analysis 1.8. Comparison 1 Non-specialist-led versus specialist-led follow-up, Outcome 8 STAI - State anxiety subscale.

Study or subgroup	Non-s	ecialist-led	Spec	ialist-led:		Mea	n Difference		Weight	Mean Difference	
	N	Mean(SD)	N	Mean(SD)		Ran	dom, 95% CI			Random, 95% CI	
Beaver 2009	144	34.9 (13.8)	132	35.7 (13.5)			#		33.73%	-0.74[-3.96,2.48]	
Beaver 2012	15	27.9 (9.8)	12	36 (17.4)			+-		2.87%	-8.1[-19.12,2.92]	
Kimman 2011	150	37.8 (10.2)	149	37.9 (10.5)					63.4%	-0.1[-2.45,2.25]	
Total ***	309		293				<b>+</b>		100%	-0.55[-2.41,1.32]	
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =	1.96, df=2(P=0.3	8); I <sup>2</sup> =0%									
Test for overall effect: Z=0.57	(P=0.57)										
			Favours	specialist-led	-50	-25	0 25	50	Favours nor	ı-snecialist	

Analysis 1.9. Comparison 1 Non-specialist-led versus specialist-led follow-up, Outcome 9 HADS - Anxiety subscale.

Study or subgroup	Non-s <sub>l</sub>	pecialist-led	Spec	ialist-led	<b>Mean Difference</b>	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI		Random, 95% CI
Brown 2002	28	5 (3)	28	7.3 (4)	<b>—</b>	10.74%	-2.24[-4.09,-0.39]
Emery 2016	39	3.5 (3.5)	43	3.7 (3.2)	<del>-</del>	15.05%	-0.2[-1.66,1.26]
Grunfeld 2006	418	5.5 (4.1)	430	5.2 (3.9)	-	34.23%	0.37[-0.17,0.91]
Kirshbaum 2017	56	6.3 (3.7)	56	5.5 (4.8)	+-	13.38%	0.85[-0.74,2.44]
Wattchow 2006	81	4 (2.6)	87	4 (3)	+	26.59%	0[-0.84,0.84]
Total ***	622		644		<b>+</b>	100%	-0.03[-0.73,0.67]
Heterogeneity: Tau <sup>2</sup> =0.3; Chi	<sup>2</sup> =8.15, df=4(P=0	.09); I <sup>2</sup> =50.92%					
Test for overall effect: Z=0.08	s(P=0.94)						
			Favours	specialist-led -10	-5 0 5	10 Favours nor	n-snecialist

Analysis 1.10. Comparison 1 Non-specialist-led versus specialist-led follow-up, Outcome 10 HADS - Depression subscale.

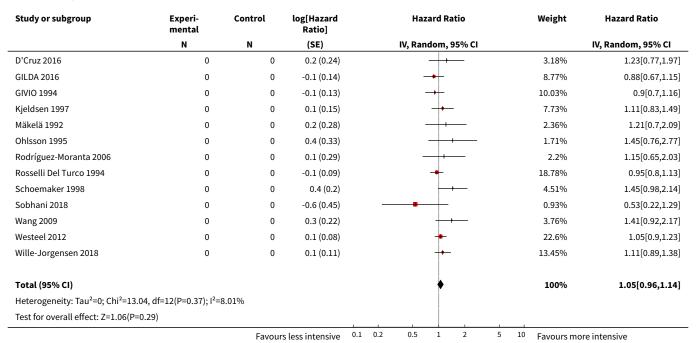
Study or subgroup	Non-s	pecialist-led	Spe	ialist-led	1	Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	F	Random, 95% CI		Random, 95% CI
Brown 2002	28	2.3 (1.8)	28	3 (2)		+	14.44%	-0.75[-1.73,0.23]
Emery 2016	39	3.3 (3.6)	43	3.7 (3.5)			6.17%	-0.4[-1.94,1.14]
Grunfeld 2006	418	3.1 (3.3)	430	2.8 (3.1)		<b>=</b>	57.45%	0.31[-0.12,0.74]
Kirshbaum 2017	56	3.4 (3.1)	56	3.6 (4)		<del>-</del>	8.18%	-0.15[-1.48,1.18]
Wattchow 2006	81	4 (3)	87	4 (3.7)		+	13.77%	0[-1.01,1.01]
Total ***	622		644			<b>\</b>	100%	0.03[-0.35,0.42]
Heterogeneity: Tau <sup>2</sup> =0.02; Ch	ii <sup>2</sup> =4.35, df=4(P=	0.36); I <sup>2</sup> =8.12%						
Test for overall effect: Z=0.17	(P=0.86)							
			Favours	specialist-led	-10 -5	0 5	<sup>10</sup> Favours nor	n-specialist



### Comparison 2. Less intensive versus more intensive follow-up

Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
1 Overall survival	13		Hazard Ratio (Random, 95% CI)	1.05 [0.96, 1.14]
2 Time-to-detection of recurrence	12		Hazard Ratio (Random, 95% CI)	0.85 [0.79, 0.92]

Analysis 2.1. Comparison 2 Less intensive versus more intensive follow-up, Outcome 1 Overall survival.



Analysis 2.2. Comparison 2 Less intensive versus more intensive follow-up, Outcome 2 Time-to-detection of recurrence.

Study or subgroup	Less in- tensive	More in- tensive	log[Hazard Ratio]	Hazard Ratio	Weight	Hazard Ratio
	N	N	(SE)	IV, Random, 95% CI		IV, Random, 95% CI
Gambazzi 2018	0	0	0.2 (0.38)	<del>-   •</del>	0.96%	1.27[0.6,2.67]
GILDA 2016	0	0	-0.2 (0.13)	<del></del>	8.18%	0.82[0.64,1.06]
GIVIO 1994	0	0	-0.1 (0.13)	+	8.18%	0.86[0.67,1.11]
Kjeldsen 1997	0	0	0 (0.16)	<del>-</del>	5.4%	1.04[0.76,1.43]
Picardi 2014	0	0	0 (0.23)	<del></del>	2.62%	1.03[0.65,1.61]
Primrose 2014	0	0	-0.3 (0.123)		9.12%	0.73[0.57,0.93]
Rodríguez-Moranta 2006	0	0	-0.1 (0.24)	<del></del>	2.4%	0.94[0.59,1.51]
Rosselli Del Turco 1994	0	0	-0.3 (0.1)	<b></b>	13.82%	0.77[0.63,0.94]
Rustin 2007	0	0	-0.3 (0.24)	<del></del>	2.4%	0.74[0.46,1.18]
Sobhani 2008	0	0	-0.2 (0.29)		1.64%	0.84[0.48,1.48]
		Favours	more intensive	0.1 0.2 0.5 1 2 5	10 Favours les	s intensive



Study or subgroup	Less in- tensive	More in- tensive	log[Hazard Ratio]			Haz	ard R	atio			Weight	Hazard Ratio
	N	N	(SE)			IV, Ran	dom,	95% CI				IV, Random, 95% CI
Westeel 2012	0	0	-0.1 (0.07)				-				28.21%	0.88[0.76,1.01]
Wille-Jorgensen 2018	0	0	-0.1 (0.09)				+				17.07%	0.87[0.73,1.04]
Total (95% CI)							•				100%	0.85[0.79,0.92]
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =6.	.83, df=11(P=0.81); I <sup>2</sup> =0%	6					İ					
Test for overall effect: Z=4.32(F	P<0.0001)											
		Favours	more intensive	0.1	0.2	0.5	1	2	5	10	Favours les	ss intensive

## ADDITIONAL TABLES

**Table 1. Summary of cost outcomes** 

Study ID	Outcome measurement	Results		
		Intervention	Comparison	
Augestad	GP-led vs surgeon-led follow-up after colon cancer	Cost per participant	Cost per participant	
	<ul> <li>The cost elements included costs related to hospital visits, GP visits, laboratory tests, radiology examinations, colonoscopy, examinations owing to suspected relapse treatment of recur-</li> </ul>	GBP 292 (255 to 327) Mean societal cost	GBP 351 (315 to 386)  Mean societal cost	
	rence, travelling/transportation, production losses, co-payments and other participant/family expenses.			
	<ul> <li>Cost minimisation analysis was carried out and reported as:</li> <li>cost per participant per 3-month follow-up cycle in GBP</li> <li>mean societal cost in GBP for 24 months' follow-up: mean (95% CI)</li> </ul>	GBP 8233 (7904 to 8619)	GBP 9889 (9569 to 10194)	
	<ul> <li>The follow-up programme initiated 1186 healthcare contacts (GP 678 vs surgeon 508), 1105 diagnostic tests (GP 592 vs surgeon 513) and 778 hospital travels (GP 250 vs surgeon 528).</li> <li>GP-organised follow-up was associated with societal cost savings (GBP 8233 vs GBP 9889, P &lt; 0.001).</li> </ul>			
Beaver 2009	Nurse-led telephone vs hospital follow-up after breast can- cer	GBP 179 (118)	GBP 24 (116)	
	<ul> <li>Resource use included training of nurses in telephone fol- low-up, routine follow-up consultations and diagnostic tests ordered, participant travel, and time of work and unit costs (e.g. salary, qualifications, ongoing training and clinic over- head)</li> </ul>			
	<ul> <li>Cost was reported as total NHS (UK) cost per participant in GBP (mean/SD) over a mean of 24 months</li> </ul>			
	<ul> <li>Owing to the cost of nurse training, greater frequency and longer duration of the telephone consultations, and the fre- quent use of junior medical staff in hospital clinics, the mean costs of follow-up consultations were higher with telephone follow-up (MD GBP 55, bias-corrected 95% CI GBP 29 to GBP 77).</li> </ul>			
Beaver 2017	Nurse-led telephone vs hospital follow-up after endometrial	6 months: GBP 434	6 months: GBP 426	
	cancer			

administration.



#### Table 1. Summary of cost outcomes (Continued)

- Unit cost data were drawn primarily from the unit costs of health and social care and NHS Reference Costs. The cost of a nurse or doctor contact hour included salary (excluding overtime and shift payments), on-costs (e.g. national insurance contributions), qualifications, the ratio of participant contact to non-contact time, and overheads.
- Unit cost data were collected from 2012/13 and inflated from the time of the study using the most recent (2016/17) UK GBP deflator so that costs were expressed in GBP at 2016/17 prices.
- Reported as total health service mean cost per participant costs at 6 months or 12 months
- Differences between groups: 6 months, GBP 8 (bias-corrected 95% GBP -147 to GBP 141); 12 months, GBP -77 (GBP -334 to GBP 154)

#### Damude 2016

#### Less frequent vs conventional follow-up schedule after melanoma

- Study authors calculated total follow-up costs of the first year for all participants from University Medical Center Groningen, Netherlands (UMCG) based on data from the UMCG financial
- Cost was reported as total cost per participant (EUR; mean/
- Study reported a reduction in hospital costs at 1-year follow-up of 45% in the intervention group compared to the conventional schedule group.

#### Grunfeld 1996

#### GP-led vs hospital follow-up after breast cancer

- The economic evaluation considered costs to the health service (particularly, the costs of follow-up visits and diagnostic tests) and costs to the participants (such as lost earnings and out-of-pocket expenses) over 18 months. All costs were expressed in 1994 GBP.
- Cost was reported as average cost per participant in GBP (95%
- GP participants were seen significantly more frequently and each follow-up visit lasted longer. GPs ordered more diagnostic tests than did specialists. Although the mean cost per visit in general practice was significantly less, the mean cost of diagnostic tests per visit was similar in the 2 groups.
- Analysis assessed the healthcare and societal costs (physician visits, diagnostic and laboratory tests, participant travel costs and lost productivity, and additional costs associated with the SCP) and QALYs over the 2-year follow-up of the randomised trial.
- - o total cost per participant in 2011 CAD
- The SCP is not cost-effective. Total costs per participant were lower for standard care (CAD 698 vs CAD 765), and total QALYs were almost equivalent (1.42 for standard care vs 1.41 for the SCP). The probability that the SCP was cost effective was 0.26 at a threshold value of a QALY of CAD 50,000.

EUR 417.66 (452.74) EUR 761.97 (683.37)

GBP 64.70 (5.80 to 301.90)

GBP 195.10 (62 to 737.40)

**CAD 698** 

**QALY 1.42** 

#### Grunfeld 2011 SCP vs no SCP after breast cancer

**QALY 1.41** 

**CAD 765** 

Cost was reported as:



#### **Table 1. Summary of cost outcomes** (Continued)

1/3	m	ma	ກ າ	A 1 1
n	шп	ша	HΖ	ULI

## Nurse-led telephone vs hospital follow-up after breast can-

· Analysis included health care (e.g. diagnostic procedures, outpatient clinic visits, telephone interviews) and nonhealthcare-related costs (e.g. productivity loss, informal care). Cost prices were obtained from the Dutch Governmen-

Costs were reported by treatment arm (see note) as:

tal manual for healthcare cost analysis.

- mean annual costs per participant in 2008 Euros (95% CI) over 12 months
- o QALY (95% CI)

Note: this study was a 4-armed 2 x 2 design that also compared the use of an educational group programme (EGP) vs no EGP. We only included the nurse-led vs hospital follow-up comparison for this review.

EUR 4672 (3489 to

6033)

EUR 4419 (3410 to

5501)

QALY 0.769 (0.746 to 0.794)

QALY 0.747 (0.707 to 0.778)

#### Koinberg 2004

#### Nurse-led on demand vs standard hospital follow-up after breast cancer

· Cost elements included medical examinations (e.g. mammography, pulmonary X-ray, scintigraphy, CT scans, US, biopsies), visits (nurse, physician, social worker, physiotherapist and breast prosthetic technician visits) and telephone con-

- Costs are reported as mean cost per participant per year of follow-up by intervention arm in 2006 Euros (95% CI) in Swe-
- Specialist nurse intervention with check-ups on demand was 20% less expensive than routine follow-up visits to the physician, explained by the numbers of visits to the physician in the respective study arms.

EUR 495 (410 to 797)

EUR 630 (557 to 1055)

Kokko 2003 Less intensive (CXR only when indicated) vs regular X-rays

after breast cancer

• Costs from the hospital perspective (no. of contacts (visits and

phone calls) and diagnostic tests) were compared during the first 5 years of follow-up

- Mean cost of follow-up per participant in 2003-2004 Euros were reported for 4 arms (see note):
  - o A: every 3 months, routine tests (X-ray every 6 months)
  - B: every 3 months, no routine tests
  - o C: every 6 months, routine tests
  - o D: every 6 months, no routine tests
- Routine examinations in the follow-up of asymptomatic primary breast cancer participants increase the costs of follow-up 2.2 times.

Note: the clinical outcomes of this study (survival and recurrence) were reported in a separate paper according to 2 groups: 1 group had regular CXRs every 6 months while the other group had CXR only when clinically needed.

## Arm B: EUR 1493

Arm A: EUR 2269

Arm D: EUR 1050

Arm C: EUR 1656

## Monteil 2010

## More intensive (CDET) vs CT scans after lung cancer

· The analysis included only direct medical costs for each participant (imaging procedure, fixed hospital and patient transEUR 1104.96 (954 to 1240)

864)

EUR 755.47 (640 to



#### **Table 1. Summary of cost outcomes** (Continued)

portation costs) over 2 years. Reimbursement prices were determined for each procedure by the French Healthcare system using 2002 repayment tariffs.

- Costs were reported as average cost of follow-up visits and imaging per participant in Euros (95% CI)
- CDET imaging was more expensive, provided earlier detection of recurrence, but did not modify survival outcome.

#### Morrison 2018

## Nurse-led telephone vs hospital follow-up after gynaecological cancer

- Mean total cost per participant (SD) of all contacts with NHS primary and secondary care services and other cancer services over the 6-month follow-up period were calculated.
- Difference between groups: GBP 26.60 (bootstrapped 95% CI GBP -290.37 to GBP 240.42)
- Although this difference is not statistically significant, the mean total costs of service use were lower in the intervention group.

## GBP 388.84 (320.11)

GBP 415.44

(329.08)

#### Oltra 2007

#### More intensive (additional diagnostic tests) vs standard follow-up after breast cancer

- Cost elements were not specified but were calculated over a median of 3 years of follow-up in a hospital in Spain where participants were recruited from 1997-1999.
- Cost reported as:
  - o total cost of follow-up in Euros
  - o mean costs per participant in Euros

#### EUR 74,171

EUR 1278 per participant EUR 24,567

EUR 390 per participant

Picardi 2014

## Less intensive (US/chest radiography) vs standard (PET/CT scans) follow-up after Hodgkin lymphoma

- Cost was calculated from the perspective of the Italian National Healthcare System including costs of imaging procedures and surgical biopsies over median follow-up of 60 months.
- Costs were reported as average cost of follow-up per participant in 2010 Euros
- Estimated cost per relapse diagnosed with routine PET/CT was 10-fold higher compared with that diagnosed with routine US/chest radiography (P < 0.0001 for difference between groups).</li>

## EUR 862

EUR 8818

#### Rodríguez-Moranta 2006

## More intensive (CT scan plus colonoscopy) vs simple follow-up after colorectal cancer

- Costs were calculated for all procedures performed during the scheduled follow-up or as a result of additional work-up for any suspected recurrence according to Hospital Clinic current billing (participants recruited from 1997-2001). Indirect costs, such as time lost from work or transportation charges, were not factored into the analysis.
- Cost were reported as:
  - cost per participant in Euros for median follow-up of up to 49 months
  - Cost per resectable tumour recurrence in Euros
- Although overall cost of follow-up was higher in the intensive strategy group (EUR 300,315) than in simple strategy group

EUR 300,315 per participant

EUR 188,630 per participant

EUR 16,684 per tu-

EUR 18,863 per tu-

mour



#### **Table 1. Summary of cost outcomes** (Continued)

(EUR 188,630), the intensive surveillance strategy was more efficient when resectability was considered.

#### Sobhani 2018

## More intensive (18FDG-PET) vs conventional follow-up after colorectal cancer

- Costs were assessed in accordance with the Consolidated
   Health Economic Evaluation Reporting Standards statement
   for single-trial-based studies.
- The prospective analysis determined the cost per life-year gained with 18FDG-PET/CT vs the standard of care over the 3year trial period. Hospital inpatient costs were estimated and average cost for each study group determined with adjustment for the actual length of stay and resources used during the admission including the cost of imaging studies. Discounting was not performed. Total cost (mean/SD) was computed both with and without the cost of 18FDG-PET/CT in 2016 EU-ROS. Costs were compared between groups using the Wilcoxon test.
- Difference between groups P value: without imaging: P = 0.23; with imaging: P = 0.033
- The probabilistic sensitivity analysis suggested that the intervention strategy increased costs without improving participant outcomes, with a likelihood of 87% for the survival end point

Without imaging: EUR 14,573 (27,531)

EUR 11,131 (13,254)

With imaging: EUR 18,192 (27,679)

#### Verschuur 2009

## Nurse-led vs surgeon-led follow-up after oesophageal cancer

- Cost elements included comprehensive data on hospital costs (inpatient days, health practitioner care, medical treatment), diagnostic interventions and extramural care (GPcare) for a period of 12 months' follow-up
- Costs were reported as total costs per participant, reported in 2006 Euros in the Netherlands
- The total average costs per participant were not statistically significantly higher for standard follow-up than nurse-led follow-up (EUR 3798 vs EUR 2592; P = 0.11). Costs of nurse-led follow-up visits were lower than those of standard follow-up visits (EUR 234 vs EUR 503; P < 0.001).</li>

EUR 2592 EUR 3798

**18FDG:** 18F-fluoro-2-deoxy-D-glucose; **CAD:** Canadian Dollar; **CI:** confidence interval; **CDET:** coincidence detection system imaging; **CT:** computed tomography; EUR: Euro; **CXR:** chest X-ray; **GBP:** Pound Sterling; **GP:** general practitioner; **MD:** mean difference; **NHS:** National Health Service; **PET:** positron emission tomography; **QALY:** quality-adjusted life year; **SCP:** survivorship care plan; **SD:** standard deviation; **US:** ultrasound

#### **APPENDICES**

### **Appendix 1. Search strategies**

Medline (OVID)

Including In-Process & Other Non-Indexed Citations



No.	Search terms	Results
1	((led or organi#e? or routine or on demand or traditional or usual or conventional or standard or patient initiate? or patient direct* or telephone? or medical or specialist? or hospital? or physician? or nurse? or oncologist? or specialist? or surg* or general practi* or family practi* or doctor?) adj2 (monitor* or follow* up or surveillance)).ti,ab.	41185
2	(follow* up adj2 (program* or appointment? or strateg* or setting? or method? or visit? or guideline? or frequen* or model? or service?)).ti,ab.	29872
3	(survivor* adj2 (follow* up or care or surveillance)).ti,ab.	3016
4	follow* up care.ti,ab.	4033
5	((shared or collaborat*) adj care).ti,ab.	3108
6	or/1-5	77900
7	(cancer* or neoplasm*).ti,ab.	1661805
8	exp neoplasms/	3107101
9	or/7-8	3536217
10	6 and 9	14878
11	((cancer* or neoplasm*) and (follow* up or surveillance)).ti.	9450
12	((cancer* or neoplasm*) adj5 (follow* up or surveillance)).ab.	17372
13	or/10-12	36753
14	exp randomized controlled trial/	472476
15	controlled clinical trial.pt.	92771
16	randomi#ed.ti,ab.	550921
17	placebo.ab.	193707
18	randomly.ti,ab.	302256
19	Clinical Trials as topic.sh.	185394
20	trial.ti.	190950
21	or/14-20	1224584
22	exp animals/ not humans/	4519948
23	21 not 22	1128470
24	13 and 23	3329



### Embase (OVID)

No.	Search terms	Results
1	((led or organi#e? or routine or on demand or traditional or usual or conventional or standard or patient initiate? or patient direct* or telephone? or medical or specialist? or hospital? or physician? or nurse? or oncologist? or specialist? or surg* or general practi* or family practi* or doctor?) adj2 (monitor* or follow* up or surveillance)).ti,ab.	62687
2	(follow* up adj2 (program* or appointment? or strateg* or setting? or method? or visit? or guideline? or frequen* or model? or service?)).ti,ab.	62362
3	(survivor* adj2 (follow* up or care or surveillance)).ti,ab.	5319
4	follow* up care.ti,ab.	5989
5	((shared or collaborat*) adj care).ti,ab.	4485
6	or/1-5	134526
7	(cancer* or neoplasm*).ti,ab.	2286996
8	exp neoplasm/	3997739
9	or/7-8	4422358
10	6 and 9	30256
11	((cancer* or neoplasm*) and (follow* up or surveillance)).ti.	13952
12	((cancer* or neoplasm*) adj5 (follow* up or surveillance)).ab.	27225
13	or/10-12	63253
14	random*.ti,ab.	1360182
15	factorial*.ti,ab.	33954
16	(crossover* or cross over*).ti,ab.	96932
17	((doubl* or singl*) adj blind*).ti,ab.	213620
18	(assign* or allocat* or volunteer* or placebo*).ti,ab.	937495
19	crossover procedure/	57588
20	single blind procedure/	33348
21	randomized controlled trial/	527339
22	double blind procedure/	156158
23	or/14-22	2083859
24	exp animal/ not human/	4495347



(Continued)		
25	23 not 24	1875090
26	13 and 25	6824

## **The Cochrane Library**

No.	Search terms	Results
#1	((led or organise? or organize? or routine or on next demand or traditional or usual or conventional or standard or (patient next (initiate? or direct*)) or telephone? or medical or specialist? or hospital? or physician? or nurse? or oncologist? or specialist? or surg* or ((general or family) next practi*) or doctor?) near/2 (monitor* or (follow* next up) or surveillance)):ti,ab	4175
#2	((follow* next up) near/2 (program* or appointment? or strateg* or setting? or method? or visit? or guideline? or frequen* or model? or service?)):ti,ab	6499
#3	(survivor* near/2 ((follow* next up) or care or surveillance)):ti,ab	286
#4	(follow* next up next care):ti,ab	465
#5	((shared or collaborat*) next care):ti,ab	802
#6	{or #1-#5}	11662
#7	(cancer* or neoplasm*):ti,ab	100585
#8	[mh neoplasms]	67779
#9	#7 or #8	126810
#10	#6 and #9	1459
#11	((cancer* or neoplasm*) and ((follow* next up) or surveillance)):ti	1361
#12	((cancer* or neoplasm*) near/5 ((follow* next up) or surveillance)):ab	1318
#13	{or #10-#12}	3542

## Cinahl (EBSCO)

No.	Search terms	Results
S1	((led or organise? or organize? or routine or on demand or traditional or usual or conventional or standard or patient initiate? or patient direct* or telephone? or medical or specialist? or hospital? or physician? or nurse? or oncologist? or specialist? or surg* or general practi* or family practi* or doctor?) N2 (monitor* or follow* up or surveillance))	13,949



(Continued)		
S2	(follow* up N2 (program* or appointment? or strateg* or setting? or method? or visit? or guideline? or frequen* or model? or service?))	8,251
S3	(survivor* N2 (follow* up or care or surveillance))	2,452
S4	follow* up care	5,632
S5	shared care or collaborat* care	10,272
S6	S1 OR S2 OR S3 OR S4 OR S5	38,036
S7	cancer* or neoplasm*	494,547
S8	(MH "Neoplasms+"	444,678
S9	S7 OR S8	552,235
S10	S6 AND S9	5,986
S11	TI ((cancer* or neoplasm*) and (follow* up or surveillance))	2,966
S12	AB ((cancer* or neoplasm*) N5 (follow* up or surveillance))	5,005
S13	(MH "Cancer Survivors")	8,872
S14	follow* up or surveillance	252,740
S15	S13 AND S14	824
S16	S10 OR S11 OR S12 OR S15	12,256
S17	S16 Limiters - Exclude MEDLINE records	2,830
S18	PT randomized controlled trial	87,221
S19	PT clinical trial	86,305
S20	TI ( randomis* or randomiz* or randomly) OR AB ( randomis* or randomiz* or randomly)	239,922
S21	(MH "Clinical Trials+")	252,999
S22	(MH "Random Assignment")	52,354
S23	S18 OR S19 OR S20 OR S21 OR S22	390,275
S24	S17 AND S23	218

## PsycINFO (OVID)

No. Search terms Results
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(Continued)		
1	((led or organi#e? or routine or on demand or traditional or usual or conventional or standard or patient initiate? or patient direct* or telephone? or medical or specialist? or hospital? or physician? or nurse? or oncologist? or specialist? or surg* or general practi* or family practi* or doctor?) adj2 (monitor* or follow* up or surveillance)).ti,ab.	3714
2	(follow* up adj2 (program* or appointment? or strateg* or setting? or method? or visit? or guideline? or frequen* or model? or service?)).ti,ab.	5259
3	(survivor* adj2 (follow* up or care or surveillance)).ti,ab.	581
4	follow* up care.ti,ab.	899
5	((shared or collaborat*) adj care).ti,ab.	1482
6	or/1-5	11300
7	(cancer* or neoplasm*).ti,ab.	56506
8	exp neoplasms/	47829
9	or/7-8	64889
10	6 and 9	1117
11	((cancer* or neoplasm*) and (follow* up or surveillance)).ti.	395
12	((cancer* or neoplasm*) adj5 (follow* up or surveillance)).ab.	793
13	or/10-12	1884
14	exp clinical trial/	11158
15	random*.ti,ab.	182773
16	((clinical or control*) adj3 trial*).ti,ab.	66395
17	((singl* or doubl* or trebl* or tripl*) adj5 (blind* or mask*)).ti,ab.	24886
18	(volunteer* or control group or controls).ti,ab.	231123
19	placebo/ or placebo*.ti,ab.	38338
20	or/14-19	426938
21	13 and 20	324

## ClinicalTrials.gov

Interventional Studies | cancer [condition] | follow up OR shared care OR surveillance [title]

## WHO International Clinical Trials Registry Platform (ICTRP)

follow up OR "shared care" OR surveillance [TITLE] AND cancer\* [CONDITION]



## Appendix 2. R code for meta-regression analyses (overall survival and time-to-detection of recurrence)

#### Overall survival

library(meta)

# dataset for Overall survival analyses.

load(data.os)

# variables list:

# study: name of study, given by first's author last name;

# logHR: logarithm of HR, considering less intense follow-up vs more intense follow-up;

# se: standard error;

# cancer: cancer type evaluated in the study;

# publication.year: publication year of the study;

# quality: quality score for the study.

# Meta-analysis (overall)

meta.os <- metagen(logHR,se,sm="HR",comb.fixed=F,studlab=study,data=data.os)

# Meta-regression for covariate CANCER

metareg.os.cancer <- with(data.os,metareg(meta.os,cancer))</pre>

# Meta-regression for covariate PUBLICATION YEAR

metareg.os.publication <- with(data.os,metareg(meta.os,publication))

# Meta-regression for covariate QUALITY SCORE

metareg.os.quality <- with(data.os,metareg(meta.os,quality))</pre>

## Time-to-detection of recurrence

library(meta)

# dataset for Time to recurrence/Disease free analyses.

load(data.ttr)

# variables list:

# study: name of study, given by first's author last name;

# logHR: logarithm of HR, considering less intense follow-up vs more intense follow-up;

# se: standard error;

# cancer: cancer type evaluated in the study;

# publication.year: publication year of the study;

# quality: quality score for the study.

# Meta-analysis (overall)

meta.ttr <- metagen(logHR,se,sm="HR",comb.fixed=F,studlab=study,data=data.ttr)

# Meta-regression for covariate CANCER

metareg.ttr.cancer <- with(data.ttr,metareg(meta.ttr,cancer))</pre>



# Meta-regression for covariate PUBLICATION YEAR

metareg.ttr.publication <- with(data.ttr,metareg(meta.ttr,publication))</pre>

# Meta-regression for covariate QUALITY SCORE

metareg.ttr.quality <- with(data.ttr,metareg(meta.ttr,quality))</pre>

Appendix 3. GRADE evidence profiles

## Certainty assessment of evidence for each outcome by comparison

1. Non-specialist-led versus specialist-led follow-up after primary cancer treatment  Certainty assessment <sup>a</sup>							Cortaintu
Nº of studies <sup>b</sup>	Study design	Risk of bias	Inconsistency	Indirectness <sup>c</sup>	Imprecision	Other considerations <sup>d</sup>	<b>Certainty</b> <sup>e</sup>
Overall surviva	al						
2	Randomised trials	Not serious	Not serious	Serious indirectness	Serious imprecision	None	<del>0</del> 000
	(4)			(-1)	(-2)		Very low
Time to detect	ion of recurrence/disea	se-free survival					
4	Randomised trials	Not serious	Serious inconsistency	Serious indirectness	Serious imprecision	None	<del>0</del> 000
	(4)		(-1)	(-1)	(-1)		Very low
Health-related	quality of life (EORTC-0	C30 - Global health	status)				
4	Randomised trials	Not serious	Serious inconsistency	Not serious	Serious imprecision	None	<del>00</del> 00
	(4)		(-1)		(-1)		Low
Anxiety (HADS	- Anxiety subscale)						
5	Randomised trials	Not serious	Some inconsistency	Not serious	Some imprecision	None	⊕⊕⊕⊝
	(4)		(-0.5)		(-0.5)		Moderate
Depresion (HA	DS - Depression subscal	le)					
5	Randomised trials	Not serious	Not serious	Some indirectness	Not serious	None	⊕⊕⊕⊕
	(4)			(-0.5)			High
Cost							
6	Randomised trials	Not serious	Serious inconsistency	Serious indirectness	Serious imprecision	None	⊕⊝⊝⊝
	(4)		(-1)	(-1)	(-1)		Very low



2. Less intensive versus more intensive follow-up after primary cancer treatment

Certainty assessment <sup>a</sup>							<b>Certainty</b> <sup>e</sup>
№ of studies <sup>b</sup>	Study design	Risk of bias	Inconsistency	Indirectness <sup>c</sup>	Imprecision	Other consid- erations <sup>d</sup>	-
Overall surviva	l						
13	Randomised trials	Some con- cerns	Not serious	Some indirectness	Serious impreci- sion	None	⊕⊕⊝⊝ Low
	(4)	(-0.5)		(-0.5)	(-1)		LOW
Time to detecti	on of recurrence/disc	ease-free surviv	al				
12	Randomised trials	Not serious	Not serious	Serious concerns	Not serious	None	⊕⊕⊕⊝
	(4)			(-1)			Moderate
Health-related	quality of life						
3	Randomised trials	Not serious	Serious inconsis-	Serious indirectness	Serious impreci-	None	<b>0000</b>
	(4)		tency (-1)	(-1)	sion (-1)		Very low
Anxiety							
1	Randomised trials	Not serious	Serious inconsis-	Serious indirectness	Serious impreci-	None	<b>0000</b>
	(4)		tency (-1)	(-1)	sion (-1)		Very low
Depression							
0	-	-	-	-	-	-	No evidence to
Cost							

(Continued)								
6	Randomised trials	Not serious	Serious inconsis-	Serious indirectness	Serious impreci-	None	<del>0</del> 000	
	(-4)		tency (-1)		sion		Very low	

(-1)

(-1)

3. Follow-up integrating additional patient symptom education or monitoring, or survivorship care plans versus usual care only								
Certainty assessment <sup>a</sup>								
№ of studies <sup>b</sup>	Study design	Risk of bias	Inconsistency	Indirectness <sup>c</sup>	Imprecision	Other consid- erations <sup>d</sup>	•	
Overall surviva	al							
0	-	-	-	-	-	-	No evidence to grade	
Time to detect	ion of recurrence/dise	ease-free surviva	al					
0	-	-	-	-	-	-	No evidence to grade	
Health-related	quality of life							
12	Randomised trials	Not serious	Serious inconsis- tency	Serious indirectness	Serious imprecision	None	⊕⊝⊝⊝ Very low	
					(-1)			
Anxiety								
	Randomised trials	Not serious	Serious inconsistency (-1)	Serious indirectness	Serious impreci- sion	None	⊕⊝⊝⊝ Very low	
	(-4)				(-1)			
Depression								
8	Randomised trials	Not serious	Serious inconsis- tency	Serious indirectness	Serious imprecision	None	⊕⊝⊝⊝ Very low	

(Continued)	(-4)	(-1)		(-1)	(-1)		
Cost							
1	Randomised trials	Not serious	Serious inconsis- tency	Serious indirectness	Serious impreci- sion	None	⊕⊝⊝⊝ Very low
	( ')		(-1)	( -/	(-1)		



#### **Footnotes**

<sup>a</sup>This can also be referred to as 'quality of the evidence' or 'confidence in the estimate'. The 'certainty of the evidence' is an assessment of how good an indication the research provides of the likely effect; that is, the likelihood that the effect will be substantially different from what the research found. By 'substantially different' we mean a large enough difference that it might affect a decision.

bFrom meta-analysis if we pooled study results for this outcome.

<sup>c</sup>Indirectness includes consideration of: indirect or between-study comparisons; indirect or surrogate outcomes; applicability, study populations, interventions, or comparisons that are different from those of interest.

dOther considerations for downgrading include publication bias. Other considerations for upgrading include a strong association with no plausible confounders, a dose response relationship, and if all plausible confounders or biases would decrease the size of the effect, if there is evidence of an effect, or increase it if there is evidence of no harmful effect (safety).

\*\*Overall score.\*\*

**High:** this research provides a very good indication of the likely effect. The likelihood that the effect will be substantially different is low. **Moderate:** this research provides a good indication of the likely effect. The likelihood that the effect will be substantially different is moderate.

**Low:** this research provides some indication of the likely effect. However, the likelihood that it will be substantially different is high. **Very low:** this research does not provide a reliable indication of the likely effect. The likelihood that the effect will be substantially different is very high.

Note: substantially different = a large enough difference that it might affect a decision.

#### **CONTRIBUTIONS OF AUTHORS**

BLH co-ordinated the review process and the drafting of the review. BLH, RVK, LS, ASF and TAH screened the titles and abstracts, appraised the included trials and extracted the data. VA, BLH and KKA were involved in the statistical analyses. All review authors contributed to th final appraisal of the included trials, the interpretation of the results and the final review for publication.

#### **DECLARATIONS OF INTEREST**

Beverley Lim Høeg (BLH), none known

Pernille Envold Bidstrup (PEB), none known

Randi Valbjørn Karlsen (RVK), none known

Anne Sofie Friberg (ASF), none known

Vanna Albieri (VA), none known

Susanne Oksbjerg Dalton, none known

Lena Saltbæk (LS), none known

 $Klaus\ Kaae\ Andersen\ (KKA), after\ completing\ the\ work\ on\ the\ review\ and\ near\ to\ its\ final\ publication,\ KKA\ started\ working\ at\ Astra\ Zeneca.$ 

Trine Allerslev Horsboel (TAH), none known

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#### SOURCES OF SUPPORT

#### **Internal sources**

• Danish Cancer Society Research Foundation, Denmark.

#### **External sources**

· No sources of support supplied

#### DIFFERENCES BETWEEN PROTOCOL AND REVIEW

**Objectives:** we have revised our objectives in order to clarify the comparisons we are evaluating. In the protocol, we had used umbrella terms of 'less intensive' and 'more intensive' follow-up to describe our main comparison. While conducting the review, it became obvious that these definitions were too broad and that an overall main comparison would not be meaningful due to the wide range of comparisons possible in studies investigating cancer follow-up. Thus, we now focus on three distinct comparisons with more stringent definitions.



**Types of studies:** we now clarify that patient-reported outcomes refer to health-related quality of life, depression and anxiety, and specify cost as an outcome in included studies.

**Types of interventions:** we have revised the description of the types of interventions so they are in line with the adjusted objectives, and thereby specify the comparisons we are making. Further, we have added a sentence specifying that we excluded studies testing only psychosocial or rehabilitation components or studies investigating components that were not integrated as part of clinical cancer follow-up. We found that necessary because it became clear that some of our searches had identified these types of studies.

**Types of outcome measures:** we have specified that in some of the included studies, time to detection of recurrence is referred to as 'disease-free survival'. We now specify the patient-reported outcomes as health-related quality of life, depression and anxiety. In the protocol, anxiety was identified as an adverse effect. In the review, we do not refer to anxiety as an adverse effect, as we cannot differentiate between the effects of the intervention and of cancer/cancer treatment on psychological distress.

**Selection of studies:** we have used Covidence instead of Endnote as the reference management system. We also updated the review authors who contributed to the screening process to include Randi Valbjørn Karlsen (RVK) and Anne Sofie Friberg (ASF).

**Data extraction and management:** we have updated the review authors who contributed to the data extraction process to include Randi Valbjørn Karlsen (RVK) and Anne Sofie Friberg (ASF).

Assessment of risk of bias in included studies: we have updated the review authors who contributed to this process to include Randi Valbjørn Karlsen (RVK) and Anne Sofie Friberg (ASF). We now assess baseline imbalances and risk of contamination under the domain 'Other bias'. We also now assess the domains 'blinding of participants and personnel', 'blinding of outcome assessment' and 'incomplete outcome data' according to objective outcomes (survival and recurrence) and patient-reported outcomes (quality of life, anxiety and depression) because objective outcomes are at lower risk of bias than self-reported outcomes. For 'blinding of outcome assessment', we further assessed the risk of bias separately for survival and time to detection of recurrence because while there can be no doubt as to death, time to detection of recurrence may be influenced by judgement regarding clinical tests and assessments, which may be affected by lack of blinding. We did not assess bias in baseline outcome measurement because this has no impact on our primary outcomes as all participants started cancer follow-up alive and cancer-free.

**Data synthesis:** we revised this part of the review according to the revised objectives. This means that data are now synthesised based on our three comparisons: 1) non-specialist-led follow-up versus specialist-led follow-up; 2) less intensive versus more intensive follow-up; and 3) follow-up integrating additional patient education/survivorship care plans relevant for detection of recurrence versus usual care. Further, we have specified that for continuous outcomes, we carried out a meta-analysis for each measurement scale or subscale that at least three studies reported at 12 months of follow-up, in order to have reasonable representativeness and probability of detecting the effect of interest.

**Subgroup analysis and investigation of heterogeneity:** we have removed 'intervention type' as a covariate, since we conducted the analyses separately based on type of intervention (according to revised objectives).

**Sensitivity analyses:** we have not performed sensitivity analyses restricted to studies with low risk of bias as stated in the protocol, since we had already investigated the effect of study quality through meta-regression.

Contributers: Anne Sofie Friberg and Vanna Albieri joined the author team for the review.

#### NOTES

This review is based on a template developed by Cochrane Effective Practice and Organisation of Care (EPOC) editorial base.

#### INDEX TERMS

## **Medical Subject Headings (MeSH)**

\*Cancer Survivors [psychology]; \*Patient Satisfaction; Anxiety [rehabilitation]; Continuity of Patient Care; Depression [rehabilitation]; Fatigue [rehabilitation]; Follow-Up Studies; Neoplasm Recurrence, Local [\*diagnosis]; Quality of Life; Randomized Controlled Trials as Topic

#### **MeSH check words**

Humans